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The Depressed Decision Maker: The Application of Decision Science to Psychopathology

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Abstract
Is decision making impaired in mental illness populations? Can behavioral economics provide insight into clinical psychology? The present project addresses these broad questions through three studies. In the first study, two meta-analyses were conducted of experiments that used the Iowa Gambling Task (IGT) to assess value based decision making in populations with mental illness. In the first meta-analysis (63 studies, combined N = 4,978), we compared IGT performance in healthy populations and populations with mental illness. In the second meta-analysis (40 studies, combined N = 1,813), we examined raw IGT performance scores as a function of type of mental illness. The first meta-analysis demonstrated that individuals with mental illness performed significantly worse than did healthy control individuals. The second meta-analysis demonstrated no performance differences based on type of mental illness. Impairment on the IGT, however, could indicate effects from several different decision processes. Accordingly, in the second study, using multiple decision tasks we explored different aspects of decision making in a single group that exhibited reliable effects in the meta-analysis, major depressive disorder. The second study answers three questions. First, how does decision making differ in clinically depressed individuals across a range of decision tasks? Second, where are the largest differences between clinically depressed and non-depressed individuals? And finally, how well can decision task performance discriminate depressed individuals from healthy controls? Depressed individuals' decision-making was significantly different across a range of decision tasks, but impaired learning and pessimism bias showed the strongest behavioral signature of depression. Decision tasks significantly predict depression, but are far outperformed by self-report measures as diagnostic tools. Overall, results suggest decision tasks are better suited to identify specific impaired processes rather than for diagnostic prediction. This study suggested depression is associated with impaired reward and punishment processing, but what are the underlying causes behind these deficits? In the third study, we performed a detailed analysis of reward and punishment learning in clinically depressed individuals, quantifying choice behavior by fitting reinforcement learning models. The results suggest that depression is characterized by hyposensitivity to reward. The reinforcement learning models show that depressed individuals engage habit-oriented model-free learning strategies in contrast to the goal-oriented model-based strategies engaged by healthy controls. Overall the three studies demonstrate how interdisciplinary research combining decision science and clinical psychology can help to better understand mental illness.

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THE DEPRESSED DECISION MAKER: THE APPLICATION OF DECISION SCIENCE TO PSYCHOPATHOLOGY

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ABSTRACT

THE DEPRESSED DECISION MAKER: THE APPLICATION OF DECISION SCIENCE TO PSYCHOPATHOLOGY

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Is decision making impaired in mental illness populations? Can behavioral economics provide insight into clinical psychology? The present project addresses these broad questions through three studies. In the first study, two meta-analyses were conducted of experiments that used the Iowa Gambling Task (IGT) to assess value based decision making in populations with mental illness. In the first meta-analysis (63 studies, combined N = 4,978), we compared IGT performance in healthy populations and populations with mental illness. In the second meta-analysis (40 studies, combined N = 1,813), we examined raw IGT performance scores as a function of type of mental illness. The first meta-analysis demonstrated that individuals with mental illness performed significantly worse than did healthy control individuals. The second meta-analysis demonstrated no performance differences based on type of mental illness. Impairment on the IGT, however, could indicate effects from several different decision processes. Accordingly, in the second study, using multiple decision tasks we explored different aspects of decision making in a single group that exhibited reliable effects in the meta-analysis, major depressive disorder. The second study answers three questions. First, how does decision making differ in clinically depressed individuals across a range of decision tasks? Second, where are the largest differences between clinically depressed and non-

depressed individuals? And finally, how well can decision task performance discriminate depressed individuals from healthy controls? Depressed individuals' decision-making was significantly different across a range of decision tasks, but impaired learning and pessimism bias showed the strongest behavioral signature of depression. Decision tasks significantly predict depression, but are far outperformed by self-report measures as diagnostic tools. Overall, results suggest decision tasks are better suited to identify specific impaired processes rather than for diagnostic prediction. This study suggested depression is associated with impaired reward and punishment processing, but what are the underlying causes behind these deficits? In the third study, we performed a detailed analysis of reward and punishment learning in clinically depressed individuals, quantifying choice behavior by fitting reinforcement learning models. The results suggest that depression is characterized by hyposensitivity to reward. The reinforcement learning models show that depressed individuals engage habit-oriented model-free learning strategies in contrast to the goal-oriented model-based strategies engaged by healthy controls. Overall the three studies demonstrate how interdisciplinary research combining decision science and clinical psychology can help to better understand mental illness.

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INTRODUCTION

Research in mental illness is beginning to shift emphasis from a symptom-based focus to a more process-based one (Sanislow et al., 2010). Mental illness is currently organized according to clinical syndromes, but critics of this approach point to notable heterogeneity within syndromes and overlapping features across syndromes. As an alternative to the syndrome approach, psychologists are increasingly studying—and sometimes even treating—basic processes that cut across traditional mental-illness categories. This crosscutting approach has begun to shape funding priorities at the National Institute of Mental Health, for example, through the recently introduced Research Domain Criteria (RDoC) proposal (Insel et al., 2010).

The present series of studies examines whether the process of value-based decision-making deserves to be included in the psychopathology-process list. We use the term value-based decision-making to denote the set of processes that is the object of study in behavioral and experimental economics and in the psychology of decision-making (including consumer behavior). We use this term to distinguish value-based decision-making both from the cognitive psychology of reasoning and judgment and from the psychophysical study of perceptual decisions. Behavioral economics examines psychological aspects of decision making by assessing the influence of social, cognitive, and emotional factors on individual economic decisions. These psychological influences affect decision-making in a way that can be captured mathematically through computational modeling techniques. The application of these tasks and techniques to psychopathology has created an emerging new field called computational psychiatry.

Two kinds of evidence suggest that processes involved in value-based decision-making might be affected by mental illness. First, the neural circuitry implicated in value-based decision making overlaps with that known to be impaired in mental illness. Studies on the neuroscience of value-based decision making have focused on the fundamental role of medial frontal and orbitofrontal cortex, striatum, amygdala, and the modulatory neurotransmitter systems that project to these regions (Bartra, McGuire, & Kable, 2013; Kable & Glimcher, 2007, 2009; Rangel & Hare, 2010). It is interesting that these very same regions also demonstrate neurochemical and functional disruption in different mental illnesses (e.g., Dom, Sabbe, Hulstijn, & Van Den Brink, 2005; Verdejo-García & Bechara, 2009; Verdejo-García, Pérez-García, & Bechara, 2006), including obsessive-compulsive disorder (OCD; Cavedini et al., 2002;Lawrence et al., 2006); depression (Grecius et al., 2007; Mayberg, 2006; Murphy et al., 2001); alcohol, cocaine, and stimulant abuse (Bechara et al., 2001; Volkow & Fowler, 2000); pathological gambling (Brand et al., 2005); and personality disorders (Raine, Lencz, Bihrle, LaCasse, & Colletti, 2000). Second, there is some empirical evidence for differences in value-based decision-making between individuals with mental illness and healthy control individuals, with examples in schizophrenia (Sevy et al., 2007), OCD (Tolin, Abramowitz, Brigidi, & Foa, 2003), substance dependence (Bechara et al., 2001; Bickel & Marsch, 2001), and depression (Clark, Chamberlain, & Sahakian, 2009).

However, despite the evidence favoring research on value based decision-making and psychopathology, certain questions remain. First, is value-based decision making *really* impaired in mental illness populations? There are qualitative reviews implicating

impairment in specific disorders but no quantitative review summarizing such a conclusion. In Study 1, we conducted quantitative meta-analyses to answer two main questions: (a) whether people with mental illness display significantly impaired value-based decision-making relative to healthy individuals, and (b) whether there are any differences in value-based decision-making across populations with different mental illnesses. The answers to these questions should inform the prospects for computational psychiatry—that is, whether or not researchers should study value-based decision making in mental illness at all and, if so, for which mental illnesses these studies might prove most important.

The first study addresses whether or not decision-making is indeed impaired in mental illness. Assuming that is the case, how can decision-making research potentially add value to the existing psychopathology literature. Based off the RDoC proposal, two areas where process based research may be useful are as classification tools and/or identifying signature behavioral markers of psychopathology. In study 2 we aim to assess value-based decision-making in a clinically depressed population with three objectives: (1) to assess potential differences in decision-making in depressed individuals compared to healthy controls, (2) to identify the largest differences in decision-making between depressed individuals and healthy controls, as well as potential underlying latent factors of decision-making, and (3) to determine the predictive accuracy of decision performance as a potential diagnostic tool.

The previous study addresses whether decision-making performance is similarly impaired across decision tasks or whether type of decision task leads to variable decision

performance. The next step investigates the underlying causes where decision performance is most compromised. Based on the results in Study 2 and literature supporting impaired reinforcement learning in depressed individuals, Study 3 was designed to examine the cause of reinforcement learning deficits in clinically depressed individuals. We analyzed reinforcement-based decision-making behavior of individuals diagnosed with depression in detail, quantifying and modeling choice behavior using reinforcement learning models. The results may inform future directions for assessment and treatment of depression.

The overarching goal of the three studies is to establish whether the process of decision-making can serve to inform and explain psychopathology in a way that is both meaningful and useful in the field of clinical psychology. In short, these preliminary investigations probe the scope and possible future direction of the study of decision-making in clinical psychology.

CHAPTER 1: VALUE-BASED DECISION-MAKING IMPAIRMENTS IN MENTAL ILLNESS: A META ANALYSIS

Abstract

In this study, we assessed value-based decision-making in individuals diagnosed with mental illness. Two meta-analyses were conducted of studies that used the Iowa Gambling Task (IGT) to assess value-based decision-making. In the first meta-analysis (63 studies, n = 4978), we compared IGT performance in healthy and mental illness populations. In the second meta-analysis (40 studies, n = 1813), we examined raw IGT performance scores as a function of type of mental illness. The first meta-analysis demonstrated that individuals with mental illness performed significantly worse than healthy controls. The second meta-analysis demonstrated no performance differences based on type of mental illness. These findings suggest that value-based decision-making is a promising target for transdiagnostic analyses of processes that go awry in mental illness. A critical priority for future work, given that impairment in the IGT could arise from changes in several decision processes, will be to investigate the specific decision processes affected in different mental illnesses.

Value-Based Decision-Making Impairments in Mental Illness: A Meta-analysis

Research in mental illness is beginning to shift emphasis away from disorder symptoms towards basic processes that can go awry across several disorders (Sanislow et al., 2010). Mental illness is currently organized according to clinical syndromes, but critics of this approach point to notable heterogeneity within syndromes and comorbidity and overlapping features across syndromes (for a more detailed review see Follette, 1996). As an alternative to the syndrome approach, psychologists are increasingly studying—and sometimes even treating—basic processes that cut across traditional mental illness categories. This crosscutting approach has begun to shape funding priorities at the National Institute of Mental Health (NIMH), for example, through the recently introduced research domain criteria (RDoC) proposal (Insel et al., 2010).

Within a process framework, one category of processes that might be worth investigating is the set involved in "value-based decision-making." We use the term value-based decision-making to denote the set of processes that is the object of study in behavioral and experimental economics and in the psychology of decision-making (including consumer behavior). We use this term to distinguish value-based decision-making both from the cognitive psychology of reasoning and judgment and from the psychophysical study of perceptual decisions.

Two kinds of evidence suggest that processes involved in value-based decision-making might be impacted by mental illness. First, the neural circuitry implicated in value-based decision-making overlaps with that known to be impaired in mental illness.

Studies on the neuroscience of value-based decision-making have focused on the fundamental role of medial frontal and orbitofrontal cortex, striatum, amygdala, and the modulatory neurotransmitter systems that project to these regions (Bartra, McGuire & Kable, 2013; Kable & Glimcher, 2007, 2009; Rangel & Hare, 2010). Interestingly, these very same regions also demonstrate neurochemical and functional disruption in different mental illnesses (e.g. Dom, Sabbe, Hulstijn, & Van Den Brink , 2005; Verdejo-García & Bechara, 2009; Verdejo-García, Pérez-García, & Bechara, 2006), including OCD (Cavedini et al., 2002; Lawrence et al., 2006), depression (Murphy et al., 2001; Grecius et al., 2007; Mayberg, 2006), alcohol, cocaine and stimulant abuse (Volkow & Fowler, 2000; Bechara et al., 2001), pathological gambling (Brand et al., 2005) and personality disorders (Raine et al., 2000). Second, there is some empirical evidence for differences in value-based decision-making between those with mental illness and healthy controls, with examples in schizophrenia (Sevy et al., 2007), OCD (Tolin, Abramowitz, Brigidi, & Foa, 2003), substance dependence (Bechara et al., 2001; Bickel & Marsh, 2001), and depression (Clark, Chamberlain, & Sahakian, 2009).

This theoretical and empirical evidence has led some researchers to propose that studies of value-based decision-making hold much promise for disentangling the fundamental processes that go awry in different forms of mental illness. Previous work on value based-decision-making in healthy individuals provides exactly the right tools – both key theoretical constructs and the laboratory tasks to measure them – needed for this effort. Montague and colleagues (2012) have even coined a name for this nascent field, "computational psychiatry," and reviewed some of the early studies employing this

research approach (for further qualitative reviews see also Cavedini, Gorini, & Bellini, 2006; Sevy et al, 2007).

Although there is reason for excitement about computational psychiatry, there also remains significant uncertainty about how fruitful this research strategy might prove to be. Most studies have compared a single mental illness population with healthy controls. The studies to date often involve small sample sizes, and this lack of power has lead to inconsistencies across studies, meaning that it is unclear whether value-based decision-making is indeed impaired in mental illness. Furthermore, given that most studies only investigate a single clinical group, and different studies use different tasks, it is unclear whether some forms of mental illness, compared with others, might demonstrate more impairment in value-based decision-making. We conducted quantitative meta-analyses to answer these two main questions, namely: (a) whether people with mental illness display significantly impaired value-based decision-making relative to healthy individuals, and (b) whether there are any differences in value-based decision-making across different mental illness populations. The answers to these questions should inform the prospects for computational psychiatry – that is, the extent to which researchers should study value-based decision-making in mental illness at all, and if so, for what mental illnesses these studies might prove most important.

To answer these questions, our meta-analyses focus on the one task sensitive to value-based decision-making processes which has been used widely across all types of mental illness, the Iowa Gambling Task (IGT; see methods for full description of the criteria and search procedure used to select the IGT). The IGT is a standardized

instrument that assesses decision-making in ambiguous situations (Bechara, Damasio, Damasio, & Anderson, 1994). In the IGT, individuals choose cards from among four decks (decks labeled A, B, C and D). Choices from two of the four decks (C and D) result in moderate gains as well as moderate losses. Choices from the other two decks (A and B) result in much higher gains as well as much higher losses. Consistent choices from decks C and D result in a net gain, while consistent choices from decks A and B result in a net loss. Thus decks C and D are considered "advantageous" while A and B are considered "disadvantageous." Performance is typically characterized by the number of choices of the advantageous decks minus the number of choices of the disadvantageous decks. Participants are unaware of these facts and must learn to maximize their monetary gain based on the feedback they receive after each choice. Typical performance evolves during the course of the task, and most healthy participants make more choices from the advantageous decks by the end of the task.

As this description should make clear, the IGT taps into many different aspects of value-based decision-making, including one's tolerance for risk and ambiguity (Holt & Laury, 2002; Ellsburg, 1961; Levy, Snell, Nelson, Rustichini, & Glimcher, 2010), the degree to which one weights losses versus gains (Kahenman & Tversky, 1979), and how well one learns on the basis of positive and negative feedback (Schönberg, Daw, Joel, & O'Doherty, 2007; Vaidya, Knutson, O'Leary, Block, Magnotta, 2007; Pessiglione, Seymour, Flandin, Dolan, & Frith, 2006). This limits the IGT's specificity in terms of the target decision process affected (at least, when overall performance is analyzed as in the studies we review, as opposed to studies that have used computational modeling to tease

apart these various factors, e.g., Ahn, Krawitz, Kim, Busemeyer, & Brown, 2011; Fridberg et al., 2010; Weller, Levin, & Bechara, 2010). However, the flip side of this lack of specificity is sensitivity to many different aspects of value-based decision-making. This sensitivity is useful for our purpose, which is to assess whether value-based decision-making processes are impaired at all in mental illness and to compare the degree of any impairment broadly across different mental illnesses. The IGT can thus serve to screen for potential impairments in value-based decision-making, and therefore provides a sensible starting point for the first quantitative comparison of value-based decision making across mental illnesses.

We performed two meta-analyses across all studies that used the IGT to assess decision-making in a mental illness population. The first meta-analysis looked at effect sizes for comparisons between healthy individuals and those with mental illness. We were particularly interested in whether there was a significant effect across all mental illnesses, and whether effect sizes reliably differed across disorders. A follow-up meta-analysis evaluated the raw scores from the IGT across different mental illnesses, rather than the differences in performance against matched healthy participants. This meta-analysis allowed a direct comparison of performance across disorders.

Methods

Selection of the IGT

Given that our goal was to assess and compare value-based decision-making across different forms of mental illness, we first searched for decision-making tasks that

had been used widely enough for this purpose. An initial PsychINFO screen through February 2011 used decision-making and specific disorders as descriptors (e.g., *decision making* and *obsessive compulsive disorder or OCD*). This broad search identified three value-based decision making tasks that had been widely used in studies of mental illness: the IGT, the Delay Discounting Task (DDT), and the Balloon Analogue Risk Task (BART). Three further searches were conducted on PsychInfo through February 2011. The first search used the following descriptors: *Delayed Discounting Task* or *Kirby Delay Discounting Measure* or *Temporal Discounting Task* or *Discounting Task* or *Probability Discounting Task*. The second search used *Balloon Analogue Risk Task* or *Balloon Analogue Risk Taking Task* as descriptors. The third search used *Iowa Gambling Task* or *IGT* as descriptor. All three searches were restricted to search the adult population (Keyword = *adult*). The selection of the final task(s) was based on two criteria – the task had been used to assess impairment across mental illness categories (e.g., OCD, mood disorder, eating disorder, substance dependence disorder, pathological gambling, schizophrenia and personality disorder) and there were at least three independent studies assessing impairment within each disorder category by using that task. We felt it was important to compare across mental illnesses with the same exact task, since different value-based decision-making tasks assess different constructs or combinations of constructs.

From these searches, we found only one task met our criteria: the IGT. Of the 40 articles reviewed that used the BART, only 3 fulfilled criteria for the present study. Of the 149 articles reviewed that used the DDT, only populations with substance

abuse/dependence were prominently featured (20 articles). A preliminary review of 282 articles using the IGT revealed that it would meet our criteria. Although we had hoped to compare mental health disorders on more than one task of value-based decision-making, the IGT provides a sensible starting point for the first quantitative comparison, as this task was used to initially identify both deficits in brain lesion populations and activations in functional imaging studies that were later proven relevant to several other tasks that assess value-based decision making.

Search Procedures

The broad clinical population under investigation prevented the use of specific and narrow search terms. Hence the behavioral task of interest, the IGT, was used as a search term and the available literature was assessed with respect to clinical pathology. Potentially relevant studies were identified via Google Scholar and PsychINFO searches through January 2012 using the descriptors *Iowa Gambling Task* or *IGT*, restricting the search to the adult population (Keyword = *adult*).

The database searches were supplemented in several ways to ensure comprehensiveness. The reference lists of relevant reviews, chapters, and articles were manually searched for potentially eligible studies. The electronic library of one of the authors (J.W.K.), who specializes in decision-making, was also searched. From a provisional list of included studies, four researchers who frequently publish relevant studies were identified, and Google Scholar and PsychInfo searches were performed using these authors' names as search terms. Several steps were also taken to address

publication bias. Unpublished dissertations were included in the PsychINFO search. The four frequent authors identified above were also contacted and asked if they had any unpublished studies pertinent to the research question. One researcher (Davis, 2011) provided unpublished data included in the study. Conference abstracts from the Society for Neuroeconomics (2005-2012), Society for Neuroscience (2000-2012) and Cognitive Neuroscience Society (2003-2012) were also searched. These abstract searches generated one additional study (Dolan et al., 2008) that fit all inclusion criteria and was included in the final meta-analyses.

Studies had to meet the following inclusion criteria to be included in either meta-analysis:

a) The study was published in English (to ensure proper coding).
b) The sample consisted only of adult participants. This ensures comparable neurodevelopmental baselines across samples.
c) For mental illness diagnosis, only studies using clinical interview methods based on the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV; APA, 1994) guidelines were used. Self-report questionnaires could not be the sole source for establishing diagnosis. This helps improve reliability and validity of a diagnosis across studies.

For inclusion in the effect size meta-analysis, studies had to additionally include a comparison group of healthy participants, and report sufficient details for an effect size to be calculated. For inclusion in the raw score meta-analysis, studies had to include the IGT net score means and SDs and/or block IGT scores and means for the clinical group under

investigation (See Supplement Material for list of references included in both meta-analyses).

Finally, to benchmark the IGT performance of mental illness populations, we compared their performance with that of brain lesion populations. Only studies using participants with ventromedial prefrontal cortex or frontal cortex lesions were selected; studies that included traumatic brain injury (TBI) were excluded. Given their known impairment on the IGT (Bechara et al., 1994; Bechara, Damasio, Damasio, & Lee, 1999; Bechara, Tranel, & Damasio, 2000), this group was included as a comparison to assess the severity of any deficits in mental illnesses.

Selection of studies

The combined search for both meta-analyses yielded 348 studies, of which 176 were retained for evaluation for inclusion (See Figure 1 and Figure 2). Of these 176 studies, six studied lesion populations and were used for comparison with mental illness populations. Sixty studies were excluded from both meta-analyses for the following reasons: described a study which did not include a clinical population (n = 15), did not include the IGT as one of its decision-making assessment tasks (n = 11), did not use interview techniques and DSM-IV guidelines to determine mental health diagnosis and/or relied on self-report measures (n = 19), were repetitions of the same sample described in another study (n = 5), were review or theoretical articles (n = 7), or included a population group other than adults (n = 3). For the effect size meta-analysis, 45 additional studies were excluded because they did not include a healthy adult comparison group (n = 29) or

they reported inadequate data for the calculation of effect sizes (n = 16). For the raw score meta-analysis, 69 additional studies were excluded because they reported inadequate data for the calculation of performance scores. Thus there were 65 articles, comprising 65 studies, that met criteria for the effect size meta-analysis and 41 articles, comprising 41 studies, that met criteria for the raw score meta-analysis. When a secondary source was available for a given study, the primary source was used to calculate the effect size unless reported data were insufficient. For comparison of effects sizes, six studies with lesion populations were available. For comparison of raw scores, only four of these studies were included as the others provided insufficient data to calculate net mean IGT performance and standard errors for lesion group. One author (Bechara et al., 1994, 1999, 2000) provided the necessary data for three of the four studies.

Coding of Studies

Given that one of our central questions was whether IGT performance varies with type of mental illness, studies were coded for both the specific type of primary mental health disorder (Obsessive Compulsive Disorders, Mood Disorders, Eating Disorders, Schizophrenia, Substance Abuse/Dependence Disorders, Pathological Gambling Disorder, and Personality Disorders) and broadly into personality vs. non-personality primary disorders. This broad distinction is of interest given the collapsing of Axis I and II disorders in the current *The Diagnostic and Statistical Manual of Mental Disorders* (5th ed.; DSM–5; American Psychiatric Association, 2013). Lack of a difference between personality and non-personality disorders would be in alignment with the collapsing of

Axis I and II categories in the DSM-5. Studies were also coded for other variables that could explain heterogeneity in effects and that were consistently reported in all studies. Since intelligence is known to affect value-based decision-making (Burks, Carpenter, Goette & Rustichini, 2009), each study was coded for whether an intelligence assessment was administered, and if intelligence was assessed, whether there was a significant difference between the clinical and healthy groups. Studies were also coded for whether the study excluded participants with substance abuse/dependence and whether the study excluded participants with traumatic brain injury or other neurological impairment (Dom et al., 2005). Comorbidity between mental disorders could be another important factor, as could whether individuals with mental health disorders are currently undergoing treatment and how long the individuals had been diagnosed with the disorder. Unfortunately, none of these factors were consistently reported across studies and so these factors could not be examined.

Independence of Effect Sizes

To meet the statistical assumption of independence of effect sizes, we took several steps to ensure that each study contributed only one effect size to each set of analyses (Lipsey & Wilson, 2001). For example, researchers may publish more than one article using the same data set or may include data used in a previous publication. Since this would violate the independence of effect sizes assumption, authors with multiple publications were contacted to provide information on whether completely independent clinical samples were recruited if they investigated the same clinical group in more than one published article. Further, in studies that included multiple clinical populations and a

single healthy control group, only the clinical population with the largest sample size was used in the effect size meta-analysis, since including multiple effect sizes calculated from the same control group would violate the independence assumption. For studies that subdivided their target clinical population into subgroups (for example, alcohol dependence with personality disorder and alcohol dependence without personality disorder) and reported data for each subgroup, the combined means and SDs for those subgroups were calculated to increase sample size and ensure independence of effect sizes.

Meta-analytic Procedures and Analyses

Weighted mean effect sizes, heterogeneity analyses and moderator analyses were conducted using Comprehensive Meta-Analysis, version 2.2.046 (Borenstein, Hedges, Higgins, & Rothstein, 2005). Since the eligible studies used different samples, and methodologies, considerable heterogeneity of effects was expected. Fixed effect models assume that the true effect size is the same in all studies, and any variability in effect sizes between studies is attributed to random error. By contrast, random effects models assume that the true effect may vary systematically from study to study. Given the expected dispersion of effect sizes, random effects analyses were used to model two aspects of the observed variance: random within-study variance and systematic between-study variance. Each effect size was weighted to account for its relative precision based on the standard error of the effect size (within-study variance) and tau-squared (between-study variance).

Effect sizes. Effect sizes for between-group comparisons were coded such that a negative effect size indicated impaired decision-making performance in the clinical group relative to the control group. Hedge's *g* (Hedges, 1981) was employed as a measure of effect size. The conventions typically used to interpret Cohen's *d* can also be applied to Hedge's *g*: an effect size of 0.2 is considered small, 0.5 is considered moderate, and 0.8 is considered large (Cohen, 1988). For studies that did not provide sufficient data for an effect size calculation but reported non-significant results, an effect size of zero was entered (Lipsey & Wilson, 2001). Given the range of study designs and purposes, methodological quality was not quantified or used in the weighting of effect sizes.

Raw Scores. For the raw score meta-analysis, performance on the IGT was expressed as the number of selections of good decks minus the number of selections of bad decks. Mean scores were calculated. Mean performance can range widely, with healthy controls typically scoring in the positive range.

Outliers. Final effect sizes or raw scores ≥ 3 SD above or below the weighted mean were identified as outliers. Two outliers were detected (Dolan, Bechara & Nathan, 2007; Dom, de Wilde, Hulstijn & Sabbe, 2007) in the effect size meta-analysis. One outlier was detected for the raw score meta-analysis (Maurex et al., 2009). The results below are presented excluding the outliers, such that the final effect size meta-analysis included 63 studies and the final raw score meta-analysis included 40 studies. The results presented here did not differ significantly when the outliers were included. Details of the three studies judged as outliers are still provided in Tables 1 and 2 below.

Publication bias. Publication bias (also called the "file drawer problem") presents a serious challenge for any meta-analysis. Studies with non-significant findings or small effect sizes have a decreased probability of being published, which can result in inflated estimates of effect size in meta-analyses of published findings. As detailed above, several steps were taken in the initial search stage to reduce the potential effect of publication bias (though admittedly these steps recovered only two unpublished studies).

We also tested statistically for the effects of publication bias in two ways. First, a funnel plot was created and visually examined. This graph plots the standard error for each study (determined by the study's sample size) against the study's effect size. The name "funnel plot" comes from the predicted presence of an inverted funnel. Studies with larger sample sizes provide more reliable estimates of the effect size and therefore should cluster more tightly around the mean toward the top of the plot, whereas smaller studies provide more variable estimates and therefore should scatter more widely around the mean toward the bottom of the plot. In the presence of publication bias, the plot becomes asymmetrical, typically with fewer small-sample-sized studies than would be predicted with effect sizes smaller than the mean. The trim-and-fill procedure was then applied to the funnel plot (Duval & Tweedie, 2000). This procedure calculates the likely number of missing studies based on the asymmetry in the funnel plot, and produces an effect size and confidence interval that is adjusted to account for these missing studies. An important caveat to the use of these procedures is that both funnel plots and the trim-and-fill procedure assume homogeneity of effect sizes. Heterogeneous datasets violate this

assumption, so the use of these techniques in such cases (which include the present cases) should be interpreted with caution.

Publication bias was also examined using classic fail-safe values (Rosenthal, 1979). The fail-safe value determines the number of missing studies with a mean effect of zero that would need to be added to the analysis before the two-tailed *p*-value would be greater than 0.05. Tolerance levels were also calculated based on the equation $5K+10$, (where K is the number of observed studies) proposed by Rosenthal (1979) to determine what would be considered an unlikely number of non-significant studies.

Homogeneity of effect sizes. The present dataset was tested for homogeneity of effect sizes using the *Q* statistic (Hedges & Olkin, 1985) and the I^2 statistic (Cooper, 2010; Higgins & Thompson, 2002; Lipsey & Wilson, 2001). The *Q* statistic has a chi-square distribution and tests whether the observed dispersion is significantly larger than the expected dispersion based on within-study error. A significant *Q* statistic suggests that the distribution of effect sizes around the mean is greater than that would be predicted from sampling error alone. The I^2 statistic estimates the percentage of the variance that is attributable to between-studies variability as opposed to within-studies sampling error. Generally percentages of $I^2 = 25$, 50, and 75 indicate low, moderate, and high degrees of heterogeneity, respectively (Higgins, Thompson, Deeks, & Altman, 2003).

Moderator analyses. Given evidence of substantial heterogeneity of effects sizes, moderator analyses were conducted on variables that might be associated with study

effects and were consistently reported across studies (see "Coding of Studies" above). Analysis of Variance (ANOVA) was conducted for categorical moderators using a mixed-effects model for each variable hypothesized to influence the effect size. This model consisted of a random-effects model, which combined studies within each subgroup, and a fixed-effect model that combined subgroups to determine the overall effect. Where applicable, the strength of differences based on moderator analyses was calculated using Cohen's *d.*

Results

Sixty-three studies contributed to the effect size meta-analysis and forty studies to the raw score meta-analysis. Study and sample characteristics are presented in Tables 1 and 2 respectively.

Results for Effect Size Meta-analysis

The results of the random-effects model for effect size indicate that mental illness populations performed reliably worse on IGT than healthy controls, with a moderately large effect size. Individual study effect sizes ranged from 0 to –1.55 (negative effect sizes indicating impaired performance in the clinical population). The average effect size was – 0.58 (95% CI – 0.68, – 0.48, $p < 0.001$). Cohen's U3 provides an intuitive metric to comprehend the magnitude of this effect size. A magnitude of – 0.58 implies that 73% of participants in the clinical population could be expected to perform worse on the IGT than the mean performance level of healthy controls (Lipsey & Wilson, 2001).

Although there was evidence of publication bias, the difference between individuals with mental illness and healthy controls was robust to this bias. The fail-safe value was 5172, far exceeding the proposed tolerance levels of what would be considered an unlikely number of non-significant studies (350). The funnel plot was asymmetric (Figure 3) with absence of potential studies on the lower right hand side of the funnel; trim-and-fill procedures suggested that 13 studies with effect sizes to the right of the mean (more strongly positive) were missing. The corrected average effect size based on the trim-and-fill procedure (Duvall & Tweedie, 2000) was – 0.44 (95% CI – 0.55 - – 0.33).

We expected heterogeneous effect sizes, since the populations comprised diverse mental illnesses. The *Q* statistic indicated significant heterogeneity among the effect sizes ($p < 0.001$). The I^2 value indicated moderate levels of heterogeneity, with 60.71% of the variance in effect sizes attributable to between-study variance.

Since the *Q* statistic and I^2 value indicated significant heterogeneity, an analysis of potential moderators was conducted to assess whether effect sizes differed on the basis of study characteristics (Table 3). Neither type of mental illness ($Q(6) = 4.60$, $p = 0.60$) nor personality/other type ($Q(1) = 1.79$, $p = .18$, $d = .34$) was a significant moderator. However, in the case of personality/other type, lack of power maybe a potential reason for the lack of significant findings. The trend was for the effect size in non-personality disorder populations, formerly Axis I disorders, ($g = –0.56$, $n = 60$) to be lower than that in personality disorder populations, formerly Axis II disorders ($g = –0.90$, $n = 3$).

A significant moderator of effect size was the assessment of intellectual functioning. Studies that did not assess intellectual functioning reported significantly more impaired decision-making performance (g = –0.86, n = 13) than studies that did assess intellectual functioning (g = –0.51, n = 50) (Q(1) = 8.58, p = 0.003, d = .35). Among the 50 studies that assessed intellectual functioning, 18 reported a significant difference in intellectual performance between the mental illness group and healthy controls. These 18 studies also used intelligence as a covariate in data analysis, which may explain why there was no difference in effect size between studies reporting a significant difference in intellectual functioning (g = –0.53, n = 18) and studies reporting no difference (g = –0.50, n = 32), (Q(1) =.12, p = 0.72, d = .03).

Neither substance use exclusion (Q(1) = .02, p = 0.90, d = .02) nor exclusion for TBI (Q(1) = .005, p = .94, d = .02) was found to be a significant moderator of effect sizes.

Finally, we compared the performance of individuals with mental illness to those with frontal lobe lesions. We combined the 63 mental illness studies with six studies involving frontal lesion groups, and did a moderator analysis with type of clinical population as a moderator (lesion vs. mental illness). Type of clinical population proved to be a significant moderator (Q(1) = 6.57, p = 0.01, d = .52) with the lesion population performing significantly worse than the mental illness population. Thus, although the mental illness group performed significantly worse than the healthy control group, their deficits were not as large as those with frontal lobe lesions (See Figure 5 for comparison of the non-personality disorder, personality disorder and lesion groups).

Results for Raw Score Meta-analysis

Performance on the IGT was quantified as the number of "good" deck choices (C + D) minus the number of "bad" deck choices (A + B). For a 100 trials this score can therefore vary from –100 to 100. Despite high variability in net IGT scores across populations, the mean net IGT score for healthy controls is usually a high net positive gain, on the order of 20 (Bechara et al., 1994), with higher scores implying better value-based decision making strategies. Mean performances for the mental illness population in individual studies ranged from –6.72 to 10.20. The average performance across all 40 studies was .45 (S.E = .88).

Though there was evidence of publication bias (Figure 4), this did not seem to have a large effect on mean performance estimates. Trim-and-fill procedures suggested that 15 studies with raw scores to the right of mean (more strongly positive) were missing. The corrected average performance was 3.74 (95% CI – 1.93 - – 5.54).

There was evidence for heterogeneity in effects across studies. The *Q* statistic indicated significant heterogeneity ($p < 0.001$). The I^2 value indicated high levels of heterogeneity, with 83.70% of the variance in raw scores attributable to between-study variance. As both statistics indicated heterogeneity, we again conducted analyses of potential moderators (Table 4). However, type of mental illness ($n = 40$) did not explain the heterogeneity in the IGT mean score (Q (6) = 2.32, $p = 0.90$). Personality disorders vs. non-personality disorders did not moderate the effect either (Q (1) = .38, $p = 0.54$, d = .84). The direction of the difference was similar to the trend observed in the effect size

meta-analysis, with non-personality disorder populations (g = 0.57, n = 38) performing better on the IGT than personality disorder populations (g = – 2.33, n = 2).

Finally, we compared the performance of individuals with mental illness to those with frontal lobe lesions. We combined the 40 studies of mental illness with four studies involving lesion groups and conducted a moderator analysis with type of clinical population as a moderator (lesion vs. mental illness). Type of clinical population proved to be a significant moderator (Q (1) = 23.35, $p < 0.001$, d = 6.62) with the populations with lesions again performing significantly worse than did the population with mental illness.

Discussion

This quantitative review answers two broad questions. The first is whether or not individuals with mental illness demonstrate impaired value-based decision-making, as assessed by the IGT, relative to healthy individuals. The effect size meta-analysis demonstrated that performance on the IGT is significantly impaired in mental illness populations, though the effect size is moderate and the deficit not as severe as in the frontal lesion population. The second question is whether, within the mental illness group, the severity of impairment differs across types of mental illness. Since different matched comparison groups might be used for different mental illnesses, the second meta-analysis, which directly compares the raw scores on the IGT in different mental illnesses, provides the clearest answer to this question. Surprisingly, the raw score meta-analysis did not demonstrate any significant differences based on type of mental illness.

The finding that value-based decision-making is significantly impaired in mental illness may not come as a surprise to most readers. Qualitative reviews of decision-making behavior in specific disorders, such as schizophrenia (Sevy et al., 2007), obsessive-compulsive disorder (Chamberlain et al., 2007), and substance use disorder (Dom et al., 2005) all align with the present findings. However, qualitative reviews can fall prey to selection or publication bias, factors that careful, quantitative meta-analyses can address. To our knowledge, the present study is the first quantitative meta-analysis to verify that value-based decision-making, as measured by any task, is consistently impaired in mental illness.

The present study is also novel in comparing value-based decision-making performance across different mental illnesses. At present, only the IGT has been tested in a wide enough range of disorders to permit such a comparison. Here our findings are perhaps more surprising: we do not find strong evidence for differential impairment on the IGT in different mental illnesses. Diagnosis was not a significant moderator in either the effect size or the raw score meta-analyses. Before we return to potential explanations for this lack of differential impairment, we first discuss two potential moderators that we did observe.

There was significant heterogeneity in size of IGT impairment across studies. Despite this heterogeneity, however, neither diagnosis nor personality vs. non-personality type moderated IGT performance in the mental illness group. There was, however, a trend in both the effect size meta-analysis and the raw score meta-analysis for people with personality disorders to be more impaired on the IGT than people with other

disorders. These findings should be interpreted with caution given that only three studies of personality disorders were included in the first meta-analysis and only two studies were included in the second. However, future studies focusing on value-based decision-making in personality disorders are warranted given the trend in the current findings. The current findings point to the possibility that people with personality disorders may experience more severe impairment than those with other disorders. This would be in line with the fact that personality disorders are more chronic and treatment resistant, while non-personality disorders usually have a more sudden onset and less prolonged time course. In fact, the IGT impairment in the small number of personality disorder studies in our meta-analyses was almost as large as that observed in patients with frontal lobe lesions, and individual studies of borderline personality disorder and antisocial personality disorder have uncovered large effects on learning from rewards or punishments (Rilling, King-Casas, & Sanfey, 2008). Given the comorbidity between personality disorders and non-personality disorders, our findings also demonstrate the importance of assessing and reporting comorbidity in future work. Indeed, it is possible that the IGT impairments observed in people with non-personality disorders in the current meta-analyses are due in part to comorbid personality disorders.

The second potential moderator, which was significant in the effect size meta-analysis was assessment of general intellectual functioning. Studies assessing intellectual functioning reported smaller levels of IGT impairment than studies that did not assess intellectual functioning. Within the studies that did assess intellectual functioning, there was no difference in the size of IGT impairment between studies that observed a

significant difference in intellectual functioning and those studies that did not find such a difference. This is likely because in those studies that did establish a significant difference, intellectual functioning was used as a covariate while assessing IGT performance. Thus, when intellectual functioning is not assessed and controlled for, the degree of decision-making impairment on the IGT appears to be inflated. These findings suggest that the IGT is sensitive to not just to value-based decision-making processes, but also to general intellectual abilities. In fact, several researchers have previously suggested that deficits on the IGT might reflect deficits in basic cognitive abilities like working memory (Hinson, Jameson, & Whitney, 2002; Jameson, Hinson, & Whitney, 2004). These findings illustrate the importance of assessing and controlling for intellectual functioning in studies of value-based decision-making. It is critical to note, however, that even when assessing and controlling for intellectual functioning, impairment on the IGT is observed in mental illness.

Returning to our central finding, why might there be widespread impairments on the IGT across all mental illnesses, with no significant evidence for differential impairments? While this null result (i.e., lack of differential impairment) should be interpreted with caution, a plausible interpretation arises from recognizing the central limitation of the current study. The IGT is only one measure, and while this measure is sensitive to many different processes involved in value-based decision-making (as well as to some general aspects of intellectual functioning, see above), it is not specific for any single decision process (Buelow & Sur, 2009). The decision literature distinguishes between many fine-grained decision processes, including aversion to risk, aversion to

ambiguity, aversion to loss, and the ability to learn from rewards and punishments (Schönberg et al., 2007; Vaidya et al., 2007; Pessiglione et al., 2006). Changes in any of these processes could have effects on IGT performance. Indeed, different groups have attributed poor IGT performance to a deficit in reversal learning (Fellows, 2007, Fellows & Farah, 2005), a preference for taking risks (Dunn, Dalgleish, & Lawrence, 2006), or insensitivity to either rewards or punishments (Franken & Muris, 2005). While it is possible that the impairments observed across different mental illnesses in the current study are all traceable back to the same underlying process within value-based decision making, it seems more likely that different mental illnesses impact different decision processes, but all of these effects lead to poorer performance on the IGT. Our findings therefore show that across mental illnesses there is impairment within the broad class of processes involved in value-based decision making to which the IGT is sensitive, but these findings do not yet identify the specific processes within that broad class that are affected by specific disorders.

A very promising avenue of future research, then, would be to assess decision-making in different mental illnesses using a wider range of tasks that more cleanly isolate specific decision processes. Studies could use a battery of tasks developed in the decision literature to assess the specific processes of risk aversion, ambiguity aversion, loss aversion, reward learning and punishment learning. To focus on two of these constructs, people might perform poorly on the IGT because they have a lower degree of risk aversion (Holt & Laury, 2002; Levy et al., 2010). That is, even once they know the probabilities and the outcomes associated with each deck, they are more willing to choose

the higher-risk (i.e., higher variance) disadvantageous decks. Alternatively, people might perform poorly on the IGT because they are slower to learn from rewards and punishments (Schönberg et al., 2007; Vaidya et al., 2007; Pessiglione et al., 2006). That is, it takes them a longer time to learn the probabilities and the outcomes associated with each deck. The decision tasks necessary to dissociate these two possibilities already exist.

In addition, performance on many of these more fine-grained decision tasks has been associated with specific neural systems. For example, neuroimaging studies using standard tasks to assess people's risk preferences have identified neural responses that scale with risk in the cingulate cortex, anterior insula, and inferior prefrontal cortex, and these neural responses predict an individual's degree of risk aversion (Christopoulos, Tobler, Bossaerts, Dolan, & Schultz, 2009; Rudorf, Preuschoff, & Weber, 2012). In contrast, individual differences in reward learning have also been identified and these are associated with neural signals in the ventral striatum that scale with reward prediction errors (Schönberg et al., 2007).

Therefore, a carefully selected battery of tasks, unlike the IGT alone, would be capable of identifying the specific "signature" of decision processes affected by a given mental illness. Comparing these signatures across mental illnesses would then permit identifying their commonalities and distinguishing features, and would furthermore lead to testable hypotheses about the neural systems affected by mental illness. Such investigations might start with those mental illnesses for which there are strong effects in the current meta-analyses, such as mood or personality disorders. This kind of study would fall squarely within the current push in clinical psychopathology towards

transdiagnostic investigations of specific psychological processes. Although such a research effort would warrant a sizable investment, the current meta-analyses suggest that such an investment would be highly likely to yield interesting, informative results.

In this light, the current meta-analyses provide a broad "screen" for possible impairments in value-based decision-making, by assessing IGT performance across mental illnesses. The obvious next step, given the widespread impairments on the IGT that we document, is to follow up on this "screen" to identify the specific decision processes that are impaired in specific disorders. Impaired decision-making is generally not a focus in psychopathology. Indeed, the DSM-5 (APA, 2013) considers decision-making impairment a possible symptom for only one disorder, major depressive disorder. The current meta-analyses suggest that further investigations of value-based decision-making in mental illness, along the lines followed in the nascent field of computational psychiatry (Montague et al., 2012), hold substantial promise for identifying specific decision processes that are adversely affected across disorders.

CHAPTER 2: THE DISCRIMINATORY POWER OF DECISION-MAKING: CAN VALUE-BASED DECISION-MAKING PREDICT AND DETECT IMPAIRED PROCESSES IN DEPRESSION?

Abstract

Incongruities between research in the biological science and clinical psychology fields validate the need to investigate underlying process-based mechanisms of mental illness. One theoretically and empirically studied cognitive process worth exploring is decision-making. The present study aims to assess value-based decision-making in a clinically depressed population with three objectives: First, to assess potential differences in decision-making in depressed individuals compared to healthy controls; second, to identify potential underlying latent factors of decision-making; and third, to determine the predictive accuracy of decision performance as a potential diagnostic tool.

Method: 128 individuals (64 clinically depressed and 64 healthy controls) were recruited. Each participant was administered a structured clinical interview, value-based decision tasks, an IQ test and several self-report questionnaires. The decision tasks used were risk aversion, ambiguity aversion, delay discounting, persistence, reward and punishment learning, the ultimatum game, and the prediction question. Independent t-tests were conducted to detect differences between the two groups. Exploratory factor analysis using promax rotation was conducted to identify potential underlying factors of decision-making. Logistic regression, including out-of-sample prediction, was used to estimate the prediction accuracy of decision performance to classify depressed and healthy individuals.

Results: Depressed participants performed significantly worse on the punishment-learning task ($p = 0.001$, $d = .58$) and reward learning task ($p = .05$, $d = .37$), were more impatient on the persistence task ($p = 0.008$, $d = .39$), made significantly less 50-50 choices in the ambiguity aversion task ($p = .04$, $d = .36$), accepted significantly less money as a responder ($p = .03$, $d = .38$) and proposed significantly more as a proposer ($p = .04$, $d = .52$) in the ultimatum game. The depressed group believed they had a significantly lower probability of winning additional money than the control group ($p = .01$, $d = .44$). Four underlying factors were identified based on decision performance – myopic decision-making, persistence, uncertainty and pessimism bias. An out of sample logistic regression using depression task scores as predictors showed a predictive accuracy of 62%.

Conclusion: Depressed individuals' decision-making performance was significantly different from healthy controls across a range of decision tasks. Potential factors of the decision process were identified and with prediction results showed learning and pessimism bias as signature behaviors of depression. Decision tasks are outperformed by self-report measures as predictive diagnostic tools. Overall results suggest decision tasks are better suited to identify specific processes gone awry rather than diagnostic prediction.

The Discriminatory Power of Decision-Making: Can Value-Based Decision-Making Predict and Detect Impaired Processes in Depression?

How depression impacts decision-making is potentially important to our understanding of both decision making and psychopathology. As depression affects 6.7% of the US adult population in a year (Kessler, Wai, Demler, & Walters, 2005), it could account for sizable heterogeneity across individual decision makers, and would therefore be of interest to economists or others interested in that heterogeneity. In addition, as depression is associated with both baseline changes in affect as well as changes in affective reactivity, the effects of depression on decision-making provide important data about how affective factors influence decision-making (Bechara, 2003; Bechara, 2004; Finucane, Alhakami, Slovic, & Johnson, 2000; Sanfey, Rilling, Aronson, Nystrom, & Cohen, 2003a; Schwarz, 2000). Thus, understanding how depressed people make monetary decisions can advance economics and decision science.

Understanding how depressed people make monetary decisions can also advance psychopathology. As illustrated for example by the Research Domain Criteria (RDoC) (Insel et al., 2010), there is increasing emphasis in psychopathology research on a nuanced understanding of the processes and mechanisms affected by mental illness, rather than only superficial clinical symptoms. Decision processes are likely an important and understudied target for these investigations. For example, a recent meta-analysis of mental illness and decision-making on one task, the Iowa Gambling Task (IGT), demonstrated impaired decision making performance across mental illnesses (Mukherjee, & Kable, 2014). In addition, the brain regions affected in psychopathology –

the frontal lobe and associated subcortical structures including the striatum and amygdala – are the same as those implicated in decision-making behavior. Depression in particular is associated with impaired functioning in ventromedial prefrontal cortex and ventral striatum, two regions known to play critical roles in value-based decision-making (Rangel, Camerer, & Montague, 2008). Using the conceptual and analytical tools of decision science to study depression could help to bridge gaps between current research in clinical psychopathology and neuroscience and behavioral science (Montague, Dolan, Friston, & Dayan, 2012).

Though several studies have begun to investigate decision making in depression, a review of the literature highlights some noteworthy gaps. First, we do not have a full characterization of how value-based decision-making differs in depressed and non-depressed individuals. Studies have demonstrated differences in value-based decision-making in depressed individuals on isolated tasks, such as the IGT (Must et al., 2006) or reward learning. But the full range of decision processes has not yet been surveyed. Are all aspects of decision-making affected or just some subcomponents? Do depressed decision makers differ in how they treat uncertainty, delay, or social demands?

Second, given that no study has investigated multiple decision processes in the same individuals with depression, we do not know yet where the biggest differences in decision making are between depressed and non-depressed individuals. Looking across a range of decision tasks could potentially identify and isolate the dimensions of the decision making processes that are most affected in depressed individuals.

Finally, we do not know how well we can successfully categorize depressed from healthy individuals based on decision performance. There is excitement about the emerging field of "computational psychiatry" (Montague et al., 2012), including the prospects for using a combination of behavioral tasks and computational models to predict and classify disorders. One study (Huys, Vogelstein, & Dayan, 2008) examined the potential of a learning task to classify depressed individuals from healthy controls. The results demonstrated significant potential. However, no studies have examined the extent of the predictive accuracy of multiple decision tasks together. How much of the depression "signal" can measures of decision making detect?

The present study seeks to address these three broad questions. How does value-based decision making differ in depressed individuals? Are some dimensions/factors of decision-making impacted more by depression than others? Finally, what is the predictive accuracy of decision-making as a diagnostic tool? To address these three questions we administered a battery of value-based decision making tasks to a sample of depressed and healthy control individuals. The selected tasks measured delayed discounting (Ainslie & Herrnstein, 1981), willingness to wait (WTW)/ persistence (McGuire & Kable, 2012), risk tolerance (Holt & Laury, 2002), ambiguity tolerance (Fox & Tversky, 1995), reward and punishment learning (Murphy, Michael, Robbins, & Sahakian, 2003), and social preferences using the ultimatum game (Sanfey, Rilling, Aronson, Nystrom, & Cohen, 2003).

Methods

Participants

Between October 2012 and January 2014, 128 participants (64 diagnosed with current Major Depressive Disorder (MDD) and 64 healthy controls) were recruited for the study. MDD participants were recruited from the Department of Psychiatry and Behavioral Health, the Counseling and Psychological Services and the Hospital of the University of Pennsylvania. A small subset of these individuals (12) agreed to be taped during the diagnostic interview for reliability purposes. Diagnostic reliability was not ascertained for the purposes of the present study as more than 80% of the individuals who participated were being referred after being given a primary diagnosis of MDD for another clinical study at Penn. Healthy control participants were recruited primarily from the staff at the University of Pennsylvania and the community through flyers. Based on an initial phone screen for depression, participants were invited for a diagnostic interview and participation in the study provided they met criteria. MDD participants were enrolled if they met the following criteria: (1) diagnostic criteria for current MDD; (2) no history of substance abuse/dependence in the past 6 months; and (3) no history of bipolar disorder and/or psychotic episodes. Diagnostic criteria were determined based on the Structured Clinical Interview for *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition* (SCID/DSM-IV) (APA, 1994). Inclusion criteria for controls included absence of current or past psychiatric illness, as assessed by the SCID, and absence of any psychotropic medications.

Groups did not differ with respect to gender, education, ethnicity, age, or IQ (Table 5). Participants in the MDD sample were moderately to severely depressed, with an average mean score of 30.03 (SD = 10.46) on the Beck Depression Inventory-II (BDI-II; (Beck, Steer, & Brown, 1996)). The mean BDI-II score for control participants was 2.9 (SD = 4.32). Within the MDD group, 41% were currently on medication and 52% were currently in treatment for depression.

Procedure

All participants provided written consent after receiving a study description. The study was approved by the Institutional Review Board at the University of Pennsylvania. The clinical interview and study procedures were conducted by a master's-level trained clinical psychologist (DM). For their participation, participants received $30 for the two hour study and possible additional payment based on their responses to one of the eight tasks. The additional payment was to ensure that the tasks had real consequences for the participants. The task chosen for additional payment was randomly selected, and participants were informed of the payment procedures prior to performance of each task. The sequence of administration was: (1) the structured clinical interview, (2) the eight decision-making tasks, with the order counterbalanced across participants according to a Latin-square design, (3) the similarities and matrix reasoning subtests of the Wechsler Abbreviated Intelligence Scale (WASI; Wechsler, 1999); (4) five self-report questionnaires; and (5) the additional payment prediction questions.

After completion of all the tasks, the participant rolled an eight-sided die to select one of the eight tasks for additional payment. For the delay discounting, risk tolerance and ambiguity tolerance tasks, one trial was selected for payment by rolling a 100-sided die, and participants were paid according to their choice on that trial. In the delay discounting task, participants were given an amazon gift card on the same day of participation but activation of the gift card depended on chosen delay (in days) for the chosen amount. For all other tasks, payment was made in cash. If participants selected the gamble in the risk tolerance task, a coin was tossed to determine whether they won or lost. For the ambiguity tolerance task, participants drew a slip of paper from the envelope they selected and were paid if they drew the winning color. Participants knew that one envelope contained 50 red and 50 blue slips of paper, while the other contained at least 25 red and at least 25 blue slips (unknown to the participant there were 49 red slips and 51 blue slips of paper). For the reward learning, punishment learning, and persistence tasks, participants were paid the total amount they won. For the ultimatum game, the participants played with actual anonymous players whose responses had already been collected. For the proposer role, the participant chose one of several responder envelopes presented to him/her. The envelopes contained the responses of an anonymous person to the responder role of the ultimatum game. If the anonymous responder accepted the proposal offered by the participant, the money was divided according to the participant's proposal. A corresponding compensation method was employed for the responder role task.

Measures

Clinical Measures. Inclusion and exclusion diagnostic criteria were based on the SCID. Depression severity was assessed with the Beck Depression Inventory (BDI- II; Beck et al., 1996). Current medication and psychotherapy treatment assessment was based on self-report.

Self-Report Measures. Several self-report measures were used to assess constructs of depression. The self-report measures used were the Rosenberg Self-Esteem Scale (RSES; (Rosenberg, 1965), the Cognitive Behavioral Avoidance Scale (CBAS; Ottenbreit & Dobson, 2004), the Behavioral Inhibition and Behavioral Activation Scale (BIS/BAS; Carver & White, 1994), and the Snaith Hamilton Pleasure Scale (SHAPS; Snaith et al., 1995). Additional measures of anxiety and depression included the Beck Anxiety Inventory (BAI; Beck & Steer, 1990) and the Depression, Anxiety and Stress Scale (Dass; Lovibond & Lovibond, 1992).

Cognitive Measures. The Wechsler Abbreviated Scale of Intelligence - Second Edition (WASI–II; Wechsler, 1999) was used as a brief, reliable measure of cognitive ability. For the purpose of efficiency, two subtests (matrix reasoning and similarities) of the WASI were implemented on each participant to obtain a full scale IQ score.

Value-Based Decision-Making Tasks

For the computerized ambiguity, risk tolerance and delay discounting tasks, the participant had two practice trial runs prior to the task. On making a choice for a trial, the task automatically moved on to the next trial. Should the participant not make a choice within 10 seconds, it automatically moved on to the next trial. Each trial was followed by

a 2-sec inter-trial interval (ITI). For the present report we focus on metrics that make the least assumptions, but we also calculated more theoretically driven measures for risk aversion (power utility function exponent), ambiguity tolerance (also a power function taking the effect of ambiguity of the perceived probability into account) and delay discounting (discount rates) and obtained similar results. Description of each task follows:

Risk Tolerance Task. The task is used to measure a participant's degree of risk tolerance. The task consisted of 51 choices. In each trial, participants were presented with the option of choosing either a smaller guaranteed amount of money or a 50% chance of winning a larger amount of money. For example, "would you choose a 50% chance of winning $35 or a sure amount of $5?" The expected value of the risky option (probability of winning times amount) could either be higher or lower than the safe amount. Performance was measured in percentage of safe options chosen.

Ambiguity Tolerance Task. The task is used to measure a participant's degree of ambiguity tolerance. The task consists of 66 choices. In each trial, participants are asked to choose between a gamble where the chances of winning are known to be 50% (risky) versus a gamble where the chances of winning are not known exactly (ambiguous). The amount won for the risky gamble is always equal to or lesser than the ambiguous gamble. Performance was measured in percentage of risky gambles chosen.

Delay Discounting Task. The task is used to measure the extent to which a participant discounts delayed rewards. The task consisted of 51 choices. Each choice was

between a smaller monetary reward available immediately and a larger monetary reward received after a delay period (in days). For example, "Would you prefer $10 now or $15 in 7 days?" Performance was calculated in percentage of now options chosen.

Persistence or Willingness to Wait (WTW) Task. In the persistence task, decision makers face the problem of optimizing persistence (in the form of waiting for a higher monetary reward) appropriately to their environment. The task is divided into two blocks, A and B. In block A, persistence leads to a higher reward, whereas in block B, continued persistence if the reward has not arrived by a certain point is suboptimal (see (McGuire, & Kable, 2012 for details). A yellow light would stay lit for a specific duration (depending on whether Block A or B condition) before delivering a 30¢ reward. Participants could choose to wait by leaving the mouse cursor in a box marked, "Wait for 30¢."Alternatively, by shifting to a box marked "Take 2¢," participants could receive 2¢ and proceed to a new trial. Each outcome (30¢ or 2¢) was followed by a 2-sec inter-trial interval (ITI). The cursor could remain in either box across multiple trials. The task was divided into two blocks (A and B), each lasting seven minutes (total duration 14 min), and the screen continuously displayed the time remaining and total earned. The optimal strategy for block A was to wait for the 30¢, while the optimal strategy for block B was to wait for the 30¢ reward for 5 secs and then take the 2¢ if the large reward had not arrived.

Individual trials provide different amounts of information about participants' willingness to wait. Quit trials are the most informative, providing a direct estimate of the limit on a participant's willingness to persist. When the reward is delivered, however, we

observe only that the person was willing to wait *at least* the duration of the trial. We accommodate this situation using statistical methods from survival analysis. Analyses assessed how long a trial would "survive" without the participant quitting.

We constructed a Kaplan-Meier empirical survival curve from each participant's responses. For each time *t*, the curve plots the probability of the participant waiting at least until *t*, provided that the reward was not delivered earlier. Analyses were restricted to the 0–11 sec interval common to the two conditions. The area under the survival curve (AUC) is a useful summary statistic, representing the average number of seconds an individual was willing to wait within the analyzed interval. Someone who never quit earlier than 11 sec would have an AUC of 11. One who was willing to wait up to 3 sec on half the trials and up to 9 sec on the other half would have an AUC of 6.

Reward Learning Task. In this task, participants choose between two distinct fractal stimuli, which are positioned randomly at two static locations (left and right of the central white dot) on screen. On each trial, participants respond by pressing a button on a keyboard to choose between the two fractals. The fractals are probabilistically rewarded; with the "richer" fractal rewarded 70% of the time and the "poorer" fractal rewarded 30% of the time. Positive feedback was provided if a fractal is rewarded (picture of a coin); otherwise, neutral feedback was provided (a red dot; indicating no coin). Participants were not informed of the specific underlying reward structure of the task. However, they were informed that on any given trial, one fractal had a higher likelihood of delivering a reward and this association reverses periodically throughout the task. All participants completed 4 trials as practice before proceeding to do a full run of 90 trials. Switches take

place after 30 trials; hence, there are two switches in total. Each reward has a monetary value of 25¢. At the end of the task, the screen displayed the total number of quarters the participant won. In this task the proportion of choosing the richer fractal image (i.e., had the higher probability of positive feedback) was calculated for each participant.

Punishment Learning Task. This task is similar to the reward learning task, except the goal for the participant is to avoid choosing the fractal leading to punishment feedback (red cross overlaying a coin). Participants are informed that at any given point, one fractal image leads to more losses than the other and that this will switch periodically. The participant starts the task with $22.50 and each time the participant chooses the fractal image followed by punishment feedback, 25¢ is deducted from the total amount. Like the reward task, participants do a 4 trial practice, before proceeding to do a full run of 90 trials, with two reversals. On completion of the task, the screen displays the total number of quarters the participant lost. Here the proportion of choosing the richer fractal image (i.e., had the higher probability of no-punishment feedback) was calculated for each participant.

Ultimatum Game, Proposer. Participants read the instructions and completed a practice quiz to ensure they understood the rules of the game. They were instructed that the game involved two people, the participant was the proposer and an anonymous person was the responder. They were informed the anonymous responder was a real person whose responses had already been recorded. As the proposer, the participant had $10 and could divide this money any way s/he wished to between himself/herself and the anonymous responder. The anonymous responder had the right to either accept or reject

the proposal. Should the proposal be accepted, the money would be divided the way the proposer decided to divide the money. However, if the proposal was rejected, neither the proposer nor the responder received any money.

Ultimatum Game, Responder. In this task, the participant played the responder's role in the ultimatum game. The participant decided whether s/he would accept or reject each possible proposal an anonymous proposer could make. Should the participant accept the proposer's division, the money would be divided accordingly.

Winning Probability or Prediction Question. Each participant responded to this questionnaire at the end of the study, prior to knowing whether or not they received additional payment. The questionnaire states, "You have now completed all the required tasks. One item will be randomly picked from one of the tasks you have performed. You may or may not receive additional money based on your response. What do you think are the chances that you will win additional money (in addition to the $30 for participation) on a scale of 0 – 100%? If you think you have an above 0% chance of winning, then how much do you think you will win in the range of $0-$100?"

Statistical Analysis

Power analysis using G*Power 3.1.2 indicated that a total of 84 participants are necessary to detect a conservatively estimated correlation= 0.30 with $\alpha = 0.05$ and $\beta = 0.80$ between the behavioral decision-making task and self-report measure for a specific component of depression (Faul et al., 2009). Power analysis using G*Power 3.1.2 determined a total of 76 participants are required to detect a moderately estimated

correlation = 0.40 with $\alpha = 0.05$ and $\beta = 0.80$, for behavioral tasks to predict overall depression using the BDI (number of regressors = 5). The current study included a total sample size of 128 individuals (64 clinically depressed and 64 healthy controls) exceeding the required 84 participants based on the power analysis.

Statistical analyses were performed using SPSS 21.0 and MATLAB 8.2. All tests were two-sided. We first compared groups on demographic and clinical characteristics using independent t-tests, one-way ANOVA and chi-square tests (Table 5). Independent *t*-tests were conducted to test significance for performance differences on each task between the two groups.

Factor Analysis.

To determine underlying latent factors captured by behavioral performance and self-reports, two separate factor analyses were conducted on the decision task performance and the self-report data using principal axis factoring using promax rotations. We also conducted a parallel analysis (Horn, 1965) to determine the number of factors to extract. Parallel analysis involves comparing the eigenvalues from the sample being analyzed to those of a randomly generated sample with the same characteristics as the sample of interest (i.e., same number of observations and variables). Factors for which the eigenvalues from the sample of interest exceed the corresponding eigenvalues from the random sample should be retained (Horn, 1965).

Decision Making Factor Analysis. The data was screened for univariate outliers. The minimum amount of data for factor analysis was satisfied, with a final sample size of

116 (using listwise deletion), providing a ratio of over 11 cases per variable. The Kaiser-Meyer-Olkin measure of sampling adequacy was .54, just above the recommended value of .5 and Bartlett's test of sphericity was significant (χ^2 (45) = 149.94, $p < .001$). The diagonals of the anti-image correlation matrix were all over .5 and the communalities were all above .3.

Self-report Factor Analysis. The data was screened for univariate outliers. The minimum amount of data for factor analysis was satisfied, with a final sample size of 125 (using listwise deletion), providing a ratio of over 12.5 cases per variable. The Kaiser-Meyer-Olkin measure of sampling adequacy was .88, above the recommended value of .5 and Bartlett's test of sphericity was significant (χ^2 (45) = 912.15, $p < .001$). The diagonals of the anti-image correlation matrix were over .5 and the communalities were all above .3.

Logistic Regression and Out of Sample Prediction.

To determine the predictive power of decision tasks relative to self-reports, logistic regression was conducted with raw scores and factor scores (from the factor analysis) for both the decision tasks and self-report measures. To quantify the accuracy of the raw score logistic models, out of sample predictions were assessed for both decision tasks and self-report. Each logistic model was tested through multiple iterations on out-of-sample individuals to estimate average correct predictive percentage. The logistic model parameters are calculated based on N number of randomly selected participants from the study (training set data). The multinomial logistic regression function in

MATLAB is used to calculate the model parameters. The parameters are then tested on the remaining participants, called test data (M – N), where M is the size of the entire data set. For the same N, the training data set is varied so that every participant is part of the test data set exactly once. We used M = 116 and N = 16. The process is repeated for 20 runs for the same value of N but for different combinations of training data set and test data set. The percentage of correctly classified participants in the test data set are calculated and averaged over the 20 runs.

Results

Demographic Characteristics

The groups were similar in their demographic characteristics (Table 5). The depressed group did not differ from the healthy control group with respect to age, gender, ethnicity or education (p values > .31). The two groups did not differ in cognitive ability (p =.35, t = .94). As expected, the MDD group reported significantly higher BDI-II scores than the healthy control group (p < .001, t = 19.33, d = 3.42).

Value Based Decision Making Performance

As compared to the healthy control group, the MDD group demonstrated significantly different decision-making on several value-based decision tasks (Table 6). In the punishment (t = 3.25, p = .001, d = .58) and reward (t = 1.98, p = .05, d = .37) learning reversal tasks, the depressed group made significantly fewer rich choices than the controls. In the ultimatum game, the depressed group offered significantly less money than the controls in the role of proposer (t = 2.10, p = .03, d = .38) and accepted

significantly less money in the role of responder ($t = 2.17$, $p = .04$, $d = .52$). In the prediction questionnaire, depressed participants reported a significantly lower expectation of winning additional money than healthy controls ($t = 2.50$, $p = .01$, $d = .44$), although the two groups did not differ in the amount of money they expected to win (average expectation = $35.50, SD = 22.52). In the ambiguity tolerance task, the MDD group made significantly less risky choices i.e., more ambiguous choices than healthy controls ($t = 2.03$, $p = .05$, $d = .36$). In the WTW task, MDD participants showed a reduced willingness to wait in block A, where the optimal strategy is to persist until the reward arrives ($t = 2.22$, $p = .03$, $d = .39$). The two groups did not differ in the number of safe options chosen in the risk tolerance task, the number of now options chosen in the delay discounting task, or in their willingness to wait in block B of the WTW task (p values > .36).

Factor Analysis

Two factor analyses were conducted on the data from the behavioral decision-making tasks and the self-report measures to determine underlying latent factors.

Decision-Making Tasks. An exploratory factor analysis using principal axis factoring with promax rotations was conducted, with four factors explaining 40.16% of the variance (Table 7). The parallel analysis indicated a three-factor solution best described the structure of the decision variables (Table 8). The scree plot indicates the presence of at least four factors (Figure 6). Since the factor analysis and the scree plot support the four-factor solution and the purpose of the current study is to determine

potential underlying dimensions (as opposed to item reduction), the four-factor solution was retained to best explain the structure. The first factor consisted of the reward and punishment reversal learning tasks and the delayed discounting task. The second factor included block A and block B of the persistence task. The third factor consisted of the ambiguity and risk tolerance tasks. The fourth factor consisted of the winning probability prediction question, and the proposer and responder roles of the ultimatum game.

To determine which of these factors, if any, were associated with depression, we ran a logistic regression model. The predictors as a set reliably distinguished depressed individuals from controls ($\chi^2 = 18.89$, $p < .001$ with df = 4). However, the Wald criterion demonstrated that only the first factor was a significant predictor ($p = .001$), though the third and fourth factors approached significance (Table 9).

Self-Report Measures. An exploratory factor analysis using principal axis factoring with promax rotations was conducted, with two factors explaining 63.62% of the variance (Table 10). Both parallel analysis (Table 11) and the scree plot (Figure 7) supported the two-factor structure. The first factor comprised of all the negative affect related questionnaires including the self-esteem, behavioral inhibition, Snaith Hamilton and cognitive-avoidance subcomponents. The underlying factor seemed to explain overall depression. The second factor consisted of positive components including the three activation BAS components in the BIS/BAS measure.

To determine which of these factors, if any, were associated with depression, we ran a logistic regression model. The predictors as a set reliably distinguished depressed

individuals from controls ($\chi^2 = 115.08$, $p < .0001$ with df = 2). The Wald criterion demonstrated that only the first factor (negative affect) was a significant predictor ($p < .0001$) (Table 12).

Logistic Regression

We conducted logistic regressions using decision performance and self-reports to determine out of sample prediction accuracy, and to isolate specific tasks or self-reports that explain unique variance in depression.

A logistic regression analysis was conducted using all of the decision tasks as predictors, and was statistically significant ($\chi^2 = 26.81$, $p < .003$ with df = 10). Nagelkerke's R^2 of .26 indicated a small relationship between prediction and grouping. The Wald criterion demonstrated that proportion of rich choices in the punishment learning task made a significant contribution to prediction ($p = .02$), while the minimum acceptance amount in the ultimatum game ($p = .053$) and winning probability ($p = .076$) trended towards significance (Table 13).

Using a step-down procedure, we created a reduced model with only significant predictors (Table 14). The reduced model contained only three predictors (punishment learning, responder in the ultimatum game, winning probability judgment). The predictors as a set reliably distinguished depressed individuals from controls ($\chi^2 = 20.97$, $p < .001$ with df = 3). We used this model to determine out-of-sample prediction accuracy for the decision tasks. Prediction accuracy was 62%, which is significantly beyond chance levels (Z = 2.37, $p = .02$, 95% CI .52 - .70).

A logistic regression analysis was conducted using the self-report measures as predictors. The predictors as a set reliably distinguished depressed individuals from controls ($\chi^2 = 131.04$, $p < .0001$ with df = 10). Nagelkerke's R^2 of .86 indicated a strong relationship between prediction and grouping. The Wald criterion demonstrated the Rosenberg Self Esteem ($p = .08$), the Snaith Hamilton ($p = .08$) and the BIS ($p = .09$) trended towards significance (Table 15).

Using a step-down procedure, we created a reduced model with only significant predictors (Table 16). The reduced model contained only three predictors (Snaith-Hamilton, self-esteem and BIS). The predictors as a set reliably distinguished depressed individuals from controls ($\chi^2 = 122.65$, $p < .000$ with df = 3). Nagelkerke's R^2 of .83 indicated a strong relationship between prediction and grouping. We used this model to determine out-of-sample prediction accuracy for self-reports. Prediction accuracy was 92%, which is significantly beyond chance levels ($Z = 9.34$, $p < .0001$, 95% CI .86 - .95).

Discussion

The first question this study addressed was how depressed individuals differ from healthy controls in value-based decision-making. Depressed individuals were less successful at learning from punishments and from rewards, offered more money as a proposer and accepted less money as a responder in the ultimatum game, believed they had a lower probability of receiving money from the experiment, had greater ambiguity tolerance, and were less persistent in waiting for delayed rewards (when persistence was

the best strategy). Depressed individuals did not differ from healthy controls in their degree of delay discounting or risk tolerance.

A factor analysis of performance across all of these tasks identified four dimensions. The first factor called myopic decision making was comprised of the learning tasks and delay discounting. These tasks may jointly identify a tendency to make decisions based on the immediate context, rather than taking prior experience or future outcomes into consideration. The second and third factors were straightforward, and were comprised of the persistence tasks and tasks measuring tolerance of uncertainty respectively. The fourth factor, bias, was comprised of the prediction question and the ultimatum game. The prediction question and the proposer role of the ultimatum game may jointly identify a tendency towards pessimistic beliefs (e.g., "I won't win," "That offer wouldn't be accepted.")

The second question this study addressed was what the biggest differences in value-based decision-making are between depressed and non-depressed individuals. The three tasks that showed the most reliable differences were punishment learning, predicting the likelihood of a positive event, and behavior as a responder in the ultimatum game. These three tasks were also the most significant predictors of depression. The three tasks accounted for distinct variance in predicting depression and loaded onto two separate dimensions in the decision performance factor analysis.

The third question this study addressed was how accurately depressed individuals could be categorized on the basis of decision performance alone. A logistic regression

model with the three most predictive tasks as regressors had an out-of-sample correct prediction accuracy of 62%. Although not dramatic, this degree of accuracy was significantly beyond chance. A logistic regression model using the self-report measures, on the other hand, showed an extremely high predictive accuracy of 92%. These results clearly demonstrate that value-based decision tasks are still a long way from the predictive accuracy of self-reports. However, we hasten to add two caveats. First, depression is determined by structured clinical interviews in which patients provide subjective reports of their symptoms. Thus it is not surprising that the written self-reports have such a high predictive accuracy, given the similarity of the constructs of the shared variance in method. Second, the goal of examining the predictive accuracy of decision performance is not to develop a diagnostic test for depression according to current diagnostic criteria, but rather to identify theoretically driven behavioral measures that may capture some of the heterogeneous differences between depressed and healthy individuals. Considering these two caveats, the significant predictive accuracy of value-based decision-making tasks we observed shows promise for future research in this area.

Interestingly, the three tasks that our results highlight as being most sensitive to depression – punishment learning tasks, probability judgment and the ultimatum game – have all been associated with depression previously. Punishment learning was the most predictive task. There is now a large body of research showing that reinforcement learning is impaired in mood disorders (Dombrovski et al., 2010; McGirr, Dombrovski, Butters, Clark, & Szanto, 2012; D. Pizzagalli et al., 2009; D. A. Pizzagalli, Iosifescu, Hallett, Ratner, & Fava, 2008). For example, in one study participants make a difficult

perceptual categorization over the course of several trials, and the probability of reward delivery is three times higher following one response versus the other. In healthy volunteers, this manipulation reliably induces a bias toward the "rich" (more frequently rewarded) response and away from the "poor" response (D. A. Pizzagalli et al., 2008). Adults with MDD develop weaker response biases. Similar results have been obtained with other reinforcement learning paradigms. Our findings suggest that reinforcement learning is the domain in which depressed individuals differ the most from controls. Given the well-established role of the dopamine system in reinforcement learning, this reinforces the critical role that changes in dopaminergic neural circuits, including targets in the ventromedial frontal lobe and ventral striatum, may play in depression (Mayberg, 1994; Tye et al., 2012).

The depressed group also differed reliably from healthy controls on the prediction questionnaire, estimating a significantly lower likelihood of winning additional payment. As the depressed group predicted a 50% probability, when the true probability was much higher, they exhibited a clear pessimistic bias. This is in alignment with previous research indicating that depressed individuals were more pessimistic in their predictions of the likelihood of future outcomes than non-depressed individuals, given identical information with which to make their forecasts (Alloy & Ahrens, 1987). The literature on optimism bias and depressive realism supports a difference between depressed individuals and controls that goes in the same direction. That this difference was apparent using only one question in the current study suggests it is reliable. Furthermore, brain activity in the

rostral anterior cingulate cortex is associated with the trait optimism while irregularities in this area are related to depression (Sharot, Riccardi, Raio, & Phelps, 2007).

Depressed individuals were also more likely to accept unfair proposals in the ultimatum game. A previous study also found that depressed individuals were more likely to accept unfair proposals (Harlé, Allen, & Sanfey, 2010). Another study did not see this effect, but did find that MDD patients offered significantly more as proposers (Destoop, Schrijvers, De Grave, Sabbe, & De Bruijn, 2012), as we find here. Depression is accompanied by clear deficits in social interaction, and a social decision making task like the ultimatum game may prove a useful tool in dissecting these deficits.

Depressed individuals were significantly different from controls in two other decision tasks, although the effects in these cases were smaller. Contrary to the avoidance behavior demonstrated by depressed individuals in daily life activities, they were more tolerant of ambiguity than controls. One possible explanation is that depressed individuals saw both gambles in this task as highly uncertain or as having low subjective probability. That is, depressed individuals may distinguish less between risk and ambiguity. As this is the first investigation of ambiguity aversion in depression to our knowledge, further replication is warranted. Future studies should also examine the generalizability of this finding beyond monetary gambles.

Unlike previous suggestions (Lempert & Pizzagalli, 2010), we did not find differences between depressed and non-depressed individuals in delay discounting. In the persistence task, however, depressed individuals were willing to wait significantly less

time for the delayed reward under conditions where persistence is the optimal strategy (Block A). No differences were observed when persistence was not the optimal strategy (Block B). Given the known role of serotonin signaling in persistence, further investigation of this effect is merited.

The results need to be interpreted in light of a couple of limitations. Though many patients were referred from depression clinics, we do not have inter-rater reliability for the depression diagnosis. We did not look at treatment and drug effects. Although we did not screen out individuals comorbid with bipolar, substance abuse and/or psychotic symptoms, we did not take other co-morbidity issues into account. Though we matched the groups on IQ, we did not include IQ in the analyses. Working memory, another potential confound, was also not taken into account. There may be other, unmeasured, confounds that differ between the two groups.

Another limitation of the study is both the clinical and control groups were combined in the sample for the factor analysis, as the sample size would have been too small for separate analyses. Because of the potential lack of homogeneity in the combined sample, the interpretation of these results should be treated with caution.

Limitations withstanding, we see two important directions in which this work could be extended. First, the current study focused on distinguishing depressed from healthy individuals. An equally important task is to distinguish different mental illnesses from each other and/or discover their commonalities. We know very little about whether and in what way decision-making measures may prove useful for this purpose. Second,

the decision measures that were most predictive in the current study may prove even more so with further refinement. There are numerous ways depressed individuals may perform poorly in punishment learning, and the other two measures were essentially single questions. Beyond refining the behavioral measures, these three tasks are also associated with distinct neural activity, and therefore may point towards brain measures that may prove even more sensitive and specific. Overall further investigation of decision making in clinically depressed individuals is warranted to better understanding the nature of clinical depression.

CHAPTER 3: REWARD? WHAT REWARD? PROBABILISTIC REVERSAL LEARNING IN MAJOR DEPRESSIVE DISORDER

Abstract

Evidence suggests that depression is associated with impaired reward and punishment processing but very little research has investigated the specific performance deficits driving poor outcomes. We analyzed reinforcement-based decision-making behavior of individuals diagnosed with depression at three levels: overt performance in terms of proportion of richer choices, specific types of choices driving performance and, finally, quantitatively modeling choice behavior based on computational reinforcement learning (RL) models.

Methods: Sixty-four clinically depressed and 64 healthy controls participated in a reward and punishment-based RL probabilistic task. Participants were compensated for their participation.

Results: Depressed individuals made significantly poorer choices on both the reward (d = .37) and the punishment (d = .58) reversal learning task. Depressed participants made significantly less win-stay choices, i.e., making the same choice, given the choice led to a reward or no punishment in the previous trial (d = 5.1 and 3.92 for punishment and reward task respectively). Choice behavior in depressed individuals was best fit by model free RL while model based learning best described choice behavior of healthy controls. Additionally, depressed individuals robustly showed a lower stimulus-learning rate controlling for action learning rate, perseveration, and choice bias.

Conclusion: The results suggest that depression is characterized by hyposensitivity to reward. The RL models suggest impaired performance was due to both cognitive deficits as well as reduced reward responsiveness in depressed individuals. The results are promising for the emerging field of computational psychiatry.

Reward? What Reward? Probabilistic Reversal Learning in Major Depressive Disorder

Depression is associated with varied symptoms ranging from mood changes to cognitive impairment (Smith, Morris, Friston, Cowen, & Dolan, 1999). Some of these symptoms may be driven at least in part by abnormal responses to affective stimuli, such as rewards and punishments (Eshel & Roiser, 2010). In the previous chapter (Mukherjee, unpublished) we saw that depressed individuals perform significantly differently from healthy controls on several decision-making tasks, but the most robust differences were in learning from rewards and punishments. Prior research corroborates our findings and shows that depressed individuals exhibit deficits in reward learning/reward bias tasks. Further, these deficits have been associated with symptoms of depression such as deriving low positive affect from pleasant events and high negative affect from unpleasant events (Brown, Chorpita, & Barlow, 1998).

Although there is strong evidence that depressed individuals are impaired at reward and punishment learning, the underlying causes behind this impairment are less clear. A goal of the present study is to examine the reasons for impaired performance in probabilistic reversal learning for rewards and punishments. There are many possible causes for impairment on these tasks. Depressed individuals may exhibit a suboptimal learning rate, reacting too slowly or too quickly to rewards and punishments. In contrast to a general hypo- or hyper-responsiveness to rewards and punishments, depressed individuals may be able to learn the initial contingencies well, but then be unable to adjust when these contingences reverse. Alternatively, depressed individuals may be less

able to take advantage of the structure of the task – that when one stimulus has a high probability of reward, the other has a low probability. This would suggest a cognitive deficit. There are several other possible explanations for poor performance that have little to do with learning reward or punishment contingencies per se. One possibility may be that depressed individuals perseverate more, i.e., once they pick an option they repeat that choice irrespective of feedback. Depressed individuals might also exhibit bias towards a particular stimulus irrespective of feedback. Finally, another possibility is that depressed individuals have stronger action-outcome associations, which are unhelpful and impede learning stimulus-outcome associations.

Previous studies have linked depression with hyposensitivity to reward as well as hypersensitivity to punishment. The results from the previous chapter (Mukherjee, unpublished) show that impaired learning is significant in both the punishment and the reward-based task, with a stronger effect for the punishment task. However, in a study a probabilistic selection task used to examine hypersensitivity to punishment in Major Depressive Disorder (MDD) patients found no significant differences between MDD patients and healthy controls (Chase et al., 2010). Other studies have found a hyposensitivity to rewards. In a probabilistic reward task, participants were asked to identify whether the mouth length of a cartoon face was short or long, with participants receiving asymmetrical rewards depending on whether correct responses were provided (Pizzagalli, Jahn, & O'Shea, 2005). Non-depressed participants learned a response bias in which the highly reinforced choice was preferred, while nonclinical depressed participants and MDD patients showed low levels of response bias (Pizzagalli et al.,

2005; Pizzagalli, Iosifescu, Hallett, Ratner, & Fava, 2008). The present study has two goals. First, does hypersensitivity to punishment, hyposensitivity to reward, or both, explain deficits in probabilistic reversal learning? The second goal is to determine whether learning is impaired for reward or punishment, or both, and to determine whether type of learning engaged by depressed individuals differs depending on reward or punishment feedback.

To achieve these goals, the present study will investigate detailed aspects of reversal learning performance in both depressed and healthy control individuals and fit computational models to assess what aspects of performance differ in the two groups. Computational modeling is a more sophisticated method of understanding learning, which has been used to study healthy individuals and individuals with organic disorders such as Parkinson's (Rutledge et al., 2009; Frank, Seeberger, & O'reilly, 2004; Daw, O'Doherty, Dayan, Seymour, & Dolan, 2006; Frank, Moustafa, Haughey, Curran, & Hutchison, 2007; O'Doherty et al., 2004), but has not yet been used to study learning behavior in depressed individuals.

Methods

Participants

Between October 2012 and January 2014, 128 participants (64 diagnosed with current MDD and 64 healthy controls) were recruited for the study. MDD participants were recruited through flyers and information provided by research assistants for patients enrolling in treatment studies in the Department of Psychiatry and Behavioral Health, and

flyers posted in the Counseling and Psychological Services at the University of Pennsylvania and the Hospital of the University of Pennsylvania (HUP). A small subset of these individuals (12) agreed to be taped during the diagnostic interview for reliability purposes. Diagnostic reliability was not ascertained for the purposes of the present study as more than 80% of the individuals who participated were being referred after being given a primary diagnosis of MDD for another clinical study at Penn. Healthy control participants were recruited from the staff and advanced students through flyers posted in the Department of Psychology, Law, and Psychiatry, the Graduate Student Office, and the HUP. Participants likely to meet study criteria based on an initial phone screen were invited for a diagnostic interview. MDD participants were enrolled if they met the following criteria (1) diagnostic criteria for current MDD, (2) no history of substance abuse/dependence in the past 6 months, (3) no history of bipolar disorder and/or psychotic episodes. Diagnostic criteria were determined based on the Structured Clinical Interview for *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition* (SCID/DSM-IV) (APA, 1994). Inclusion criteria for controls included absence of current or past psychiatric illness, as assessed by the SCID, and the absence of any psychotropic medications.

All participants provided written consent after receiving a study description. The study was approved by the Institutional Review Board at the University of Pennsylvania. The clinical interview and study procedures were conducted by a master's level trained clinical psychologist (DM). The data we report here from the reward and punishment reversal-learning tasks were collected as part of a larger research study investigating

value-based decision-making in individuals diagnosed with MDD. Participants were paid $15/hr. They received additional incentive based on their choices in *one* randomly selected decision task out of the eight administered. The sequence of administration of the various components of the study took place in the following order – administration of the structured clinical interview, performance on the eight decision-making tasks (including the reward and punishment probabilistic reversal learning tasks), performance on the similarities and matrix reasoning subtests of the Wechsler Abbreviated Intelligence Scale (WASI; Wechsler, 1999), and completion of self-report measures.

Measures

Clinical Measures. Inclusion and exclusion diagnostic criteria were based on the SCID. Depression severity was assessed with the Beck Depression Inventory (BDI; Beck et al., 1996). Current medication and psychotherapy treatment assessment was based on self-report.

Cognitive Measure. The Wechsler Abbreviated Scale of Intelligence - Second Edition (WASI–II) provides a brief, reliable measure of cognitive ability. For the purpose of efficiency, two subtests (matrix reasoning and similarities) of the WASI were administered to each subject to obtain a full scale IQ score.

Reward Probabilistic Reversal Learning Task. In this task, subjects choose between two distinct fractal stimuli (Figure 8), which are positioned randomly at one of two locations (left and right of the central white dot) on screen. On each trial, participants respond by pressing a button on a keyboard to choose between the two fractals. Positive

feedback is provided if a fractal is reinforced with a reward (picture of a quarter); otherwise, neutral feedback is provided (a red dot). The fractals are probabilistically rewarded; with the richer fractal rewarded 70% of the time and the poorer fractal rewarded 30% of the time. Participants are not informed of the specific underlying reward structure of the task. However, they are informed that on any given trial, one fractal has a higher likelihood of delivering a reward and that this association reverses periodically throughout the task. All participants complete 4 trials as practice before proceeding to do a full run of 90 trials. The 90 trials are divided into three blocks of 30 trials each. At the end of 30 trials a reversal takes place, i.e. the image which had the higher reward probability now has the lower reward probability and vice versa. Each reward has a monetary value of $0.25. At the end of the task, the screen displays the total number of quarters the participant won.

Punishment Probabilistic Reversal Learning Task. This task is similar to the reward probabilistic reversal learning task except the goal for the participant is to try to avoid choosing the fractal leading to punishment (signified by red cross overlaying a quarter) (Figure 8). Participants are informed that at any given point, one fractal image leads to more losses than the other and that this will switch periodically. The participant starts the task with $22.50 and each time the participant chooses the fractal image followed by punishment feedback, $0.25 is deducted from the initial total amount ($22.50). Like the reward task, subjects do a 4 trial practice, before proceeding to do a full run of 90 trials, with two reversals. On completion of the task, the screen displays the

total number of quarters the participant lost, and wins $22.50 minus the total number of lost quarters.

Performance Analysis

Aspects of performance measured in both groups were, (1) average proportion of rich choices made, (2) proportion of win-stay choices and lose-shift choices, and (3) proportion of win-stay and lose-shift choices broken down by whether the fractals were presented on the same side or different sides in consecutive trials. Rich choices were choices of the fractal with the higher probability of reward (for the reward-learning task) or the higher probability of no punishment (for the punishment-learning task). A win-stay choice is when a participant repeats the same choice (chose the same fractal image) when making that choice in the previous trial led to a win (reward or no punishment). A lose-shift choice is when the participant switches his/her choice (chose a different fractal image) when the choice in the previous trial led to no reward (in the reward-learning task) or to punishment (in the punishment-learning task). Win-stay and lose-shift choices were also analyzed separately depending on whether the fractals were presented on the same sides in consecutive trials or whether the fractals switched sides.

Linear Regression Model

In order to test whether the choice behavior of participants was consistent with reinforcement learning, we first fit a linear regression to choice data (Lau & Glimcher, 2008). We assumed that influences of past rewards were linearly combined to determine choice on each trial, with choice probability computed using the softmax rule. We used

logistic regression to estimate weights for rewards received and choices made on previous trials. The goal of the regression was to estimate the probabilities of choosing the fractal 1 image, P_{F1}(t), and the fractal 2 image, P_{F2}(t), respectively. Since there are only two options, we assume symmetric weights for the two options, and the model for 10 previous rewards and one previous choice reduces to the following:

$$\log\left(\frac{P_{F1}(t)}{P_{F2}(t)}\right) = \sum_{i=1}^{10} a_i (R_{F1}(t-i) - R_{F2}(t-i)) + b(C_{F1}(t-1) - C_{F2}(t-1)) + c \qquad (1)$$

Here, the coefficients a_i and b represent changes in the log odds of choosing fractal 1 and fractal 2 options with a_i the weight for a reward received i trials ago, b is the weight for the last choice made. Positive weights indicate increases in the log odds of choice as a function of previous rewards (a_i) or last choice. The log odds of the subject making a given choice on a specific trial is obtained by linearly combining outcomes (rewards), weighted by the coefficient extracted by the regression and a bias factor c. Behavior consistent with RL should demonstrate an exponential decline of the influence of past rewards. The linear regression model thus relaxes the constraint imposed by the reinforcement learning models that weights must decline exponentially, which enables us to examine the robustness of this assumption.

Reinforcement Learning Models

Finally, we fit different computational models to examine how these could account for aspects of performance that differed between the two groups. Computational models were fit with the function minimization tools in MATLAB.

Model Free RL

We first fit choice data from all subject groups with a standard reinforcement learning model (Sutton & Barto, 1998). The model uses the sequence of choices and outcomes to estimate the expected value of each option for every trial. The expected values are set to zero at the beginning of the experiment, and after each trial, the value of the chosen option (for example, $V_{F1}(t)$ for fractal 1 option at trial *t*) was updated according to the following rule:

$$V_{F1}(t+1) = V_{F1}(t) + \alpha_s \delta_s(t) \quad (2)$$

$$\delta_s(t) = R_{F1}(t) - V_{F1}(t) \quad (3)$$

Here, $\delta_s(t)$ is the stimulus reward prediction error (RPE), the difference between the experienced and the expected reward. $R_{F1}(t)$ represents the outcome received from the fractal 1 option on trial *t* with a value of 1 for a reward and 0 otherwise. The learning rate α_s determines how rapidly the estimate of expected value for the fractal image chosen is updated. If the learning rate is high, recent outcomes have a relatively greater influence on the expected value than less recent outcomes.

This model also included other parameters that are not helpful for learning but that our analysis of the performance metrics indicated could potentially be influencing choice behavior. These added parameters included a term for choice perseveration, a term of bias towards one stimulus, and two terms (learning rate and noise) for action learning.

Action learning is similar to the above model except that here the model uses the sequence of actions (left/right button presses rather than fractals chosen) and outcomes to estimate the expected value of each action for every trial. The expected values are set to zero at the beginning of the experiment, and after each trial, the value of the chosen action (for example, $V_L(t)$ for the left hand option at trial *t*) was updated according to the following rule:

$$V_L(t+1) = V_L(t) + \alpha_a \delta_a(t) \quad (4)$$

$$\delta_a(t) = R_L(t) - V_L(t) \quad (5)$$

Here, $\delta_a(t)$ is the action reward prediction error (RPE), the difference between the experienced and the expected reward. $R_L(t)$ is the outcome received from using the left hand on trial *t* with a value of 1 for a reward and 0 otherwise. The learning rate α_a determines how rapidly the estimate of expected value is updated. If the learning rate is high, recent outcomes have a relatively greater influence on the expected value of than less recent outcomes.

Choice is theoretically a function of expected stimulus value. We can combine the stimulus and action based models into a six parameter model to reflect the influence of both types of learning parameters in a dual model. Given the expected values for both fractal options, the probability of choosing fractal 1 option $P_{F1}(t)$ is computed using the following softmax rule:

$$P_{F1}(t) = \frac{1}{1+\exp\{-\beta_s\left(V_{F1}(t)-V_{F2}(t)\right)+\beta_a\left(V_L(t)-V_R(t)\right)+... \\ ... \; c\left(C_{F1}(t-1)-C_{F2}(t-1)\right)+d\left(D_{F1}(t-1)-D_{F2}(t-1)\right)\}} \quad (6)$$

Here, β_s is the noise parameter for stimulus, β_a is the noise parameter for action learning $V_{F1}(t)$ and $V_{F2}(t)$ are the values of fractal 1 and fractal 2 on trial *t* respectively, $V_L(t)$ and $V_R(t)$ is the values for choosing the left and the right hand respectively at trial *t*, $C_{F1}(t-1)$ and $C_{F2}(t-1)$ represent the choice of fractal 1 and fractal 2 on the presvious trial *t* – 1 respectively, with a value of 1 for the chosen option and 0 otherwise i.e. $C_{F1}(t)=1-C_{F2}(t)$, $D_{F1}(t-1)$ and $D_{F2}(t-1)$ represent the bias towards fractal 1 and fractal 2 on the previous trial t – 1 respectively, with a value of 1 for the chosen option and 0 for the option not chosen.

The dual RL model consisted of six parameters - α_s (stimulus based learning rate), α_a (action based learning rate), β_s and β_a (noise parameters), *c* (choice perseveration parameter), and *d* (bias parameter) and were estimated by maximum likelihood (Burnham & Anderson, 2002).

Model based RL

We also fit a second variation of the model that involved an update of both the chosen and unchosen options in the stimulus-based learning equation. This model approximates a model-based Bayesian learner, because it takes into account the structure of the task and the fact that the reward probabilities on the two options are anti-correlated. Stimulus values are updated using the following rule:

RPE	$\delta_{F1}(t) = R_{F1}(t) - V_{F1}(t)$	(7)
Chosen Value	$V_{F1}(t+1) = V_{F1}(t) + \alpha\delta_{F1}(t)$	(8)
Unchosen Value	$V_{F2}(t+1) = -V_{F1}(t) + \alpha\delta_{F2}(t)$	(9)

The new value at trial $t+1$ for the currently chosen fractal is based on the sum of the observed prediction V_{F1} and the prediction error $R_{F1}(t) - V_{F1}(t)$ whereas the value for the unchosen option V_{F2} is based on a fictitious prediction error $-V_{F1}(t) + \alpha\delta_{F2}(t)$ that takes the counterfactual outcome for the current trial into account. In this model α is the learning rate, i.e., the influence of both prediction errors on the value update. The inclusion of an update rule for the unchosen option captures an important feature of the task structure, namely that the choice values are anti-correlated. This update rule incorporates the knowledge the participants have that when the action they are choosing increases or decreases in value, the value of the option they are not choosing does the opposite.

Model Comparison

To compare the RL models, we penalized model fits for complexity using the Bayesian information criterion (BIC; Schwarz, 1978). We computed BIC using the following equation:

$$\mathrm{BIC} = -2\log L + k\log n \quad (10)$$

Here, L is the maximum log likelihood for the estimated model given the data, k is the number of free parameters in the model, and n is the number of trials. Models with lower BIC are preferred.

Statistical Analysis

Statistical analyses were performed using SPSS 21.0 and MATLAB 8.2. All tests were two-sided. We first compared groups on demographic and clinical characteristics using independent t-tests, one-way ANOVA and chi-square tests (Table 17). Performance metrics were compared between the two groups or within groups using independent t-tests.

Results

Demographic Characteristics

Groups did not differ with respect to gender, education, ethnicity, or age (p values above .3, Table 17). The groups did not differ in cognitive ability (p = .35). Participants in the MDD sample were moderately to severely depressed, with a significantly higher average BDI–II mean score of 30.03 (SD = 10.46) than control subjects was (M = 2.9, SD = 4.32, $p < .001$). Within the MDD group, 41% and 52% were on current medication or in treatment for depression, respectively.

Behavioral Performance Results

Depressed individuals performed significantly poorer on both reward and punishment reversal learning. In the reward reversal learning task depressed participants (M = 59.59%, SD = 9.84) made significantly fewer rich choices than the controls (M = 63.21%, SD = 10.80, $p = .05$). This was true for the punishment task also. In the punishment reversal-learning task, the depressed participants (M = 58.49%, SD = 9.93) made significantly fewer rich choices than the controls (M = 64.56%, SD = 10.81, $p = .001$, Figure 9).

These deficits appear during initial learning and continue throughout the task, a pattern inconsistent with a specific inability to reverse learned contingencies. In the reward task, we see controls perform better than the depressed group across all three blocks, with significant differences from trials 30 through 57 and 72 through 77 (p values < .04, Figure 9). For the punishment-learning task, we see a similar pattern (Figure 9). The depressed group chose significantly less rich choices from the beginning, with significant differences from trials 12 through 23, 32 through 57 and finally 74 through 85 (p values < .01).

We next examined whether behavior in the two groups was consistent with reinforcement learning by measuring a participant's win-stay and lose-shift choices. Specifically, behavior consistent with RL would evidence a high proportion of win-stay choices. In the reward learning task, the average proportion of win-stay choices for both groups was above 50%, but was significantly less for the depressed group (M = .74, S.E = .03) than the control group (M = .84, S.E = .02, $p = .03$) (Figure 10). No significant differences were observed for lose-stay choices with both groups shifting approximately

50% of the time after experiencing no reward in the preceding trial. A similar pattern was observed in the punishment learning task. The average proportion of win-stay choices was greater than 50% in both groups, but significantly less in the depressed group (M = .71, S.E = .03) compared to the control group (M = .83, S.E = .02, $p < .001$) (Figure 10). Again, there were no significant differences for the lose-shift proportions. The high proportion of win-stay choices in both groups in both tasks is consistent with reinforcement learning. However, the controls were more responsive to positive feedback in both tasks, suggesting the depressed group may be less sensitive to positive outcomes.

Looking at win-stay versus lose-shift choices according to whether the specific motor response repeated or not (fractals were on the same side vs. different side across trials) revealed a potential influence of action learning on task performance. In the reward learning task, a within group comparison demonstrated both depressed and control individuals were significantly more likely to win-stay and lose-shift when the specific motor action repeated across trials (p's <.05). The punishment task results showed a similar significant pattern (p's <.05) for win stay and lose shift action association (Figure 10). In short, both groups engaged in action outcome learning.

To more rigorously check whether choice behavior was consistent with reinforcement learning, we fit trial-by-trial choice data using a linear regression model (Figure 11). Reinforcement learning models assume the influence of rewards from previous trials decays in an exponential manner determined by the learning rate (α). The linear regression fits show behavior was consistent with reinforcement learning in both tasks in both groups. The first two parameters were above zero for both groups in both

tasks, and higher weight was assigned to the reward received in the preceding trial compared to rewards received two trials back (*p's* < .0001). The fits also suggest that the control group learns at a faster rate, as a higher weight was assigned to the most recent trial in the control group than in the depressed group (reward task, $t = 9.31$, $p < .0001$; punishment task, $t = 9.67$, $p < .0001$).

We next analyzed whether computational models could capture these aspects of performance, including the difference between the two groups. We first compared the model-free versus model-based reinforcement learning algorithms. Model-free learning only updates the value of the chosen option, while model based learning implies both chosen and unchosen values are updated. The model-based algorithm thus takes into account the structure of the task, that reward probabilities on the two fractals are anticorrelated. Given the observed effects of repeating the motor action on win-stay and lose shift choices in both groups, we also included a (model-free) action learning component in the model, as well as terms for choice persistence and bias towards one of the fractals.

Two major differences were detected between the groups. First, for both the reward and punishment learning tasks, model-based reinforcement learning fit the choice data for the control group better than model-free reinforcement learning, while the reverse was true in depressed individuals (Table 18). Second, irrespective of model-based versus model-free, the one component of the model that significantly differed across groups was the learning rate (Table 19). Models that assumed that depressed and control subjects had different learning rates consistently fit the choice data better, while this was

not the case for action learning, persistence, or bias parameters. In the reward task, the best fit learning rate for controls is .73 while for depressed individuals it was .41; for the punishment task, the learning rates were .71 and .37 for controls and depressed respectively. Thus, for both tasks depressed individuals demonstrate a lower learning rate than controls.

Discussion

In this study we show why depressed individuals learn from rewards and punishments poorer than controls. Our analyses of performance and computational modeling of behavior revealed two interesting differences. First, depressed individuals are more likely to engage in model-free reinforcement learning while controls are more likely to use the structure of the task and engage in model-based reinforcement learning. Second, regardless of whether learning is model-free or model-based, depressed individuals have a lower learning rate than controls. These two differences held irrespective of whether the task involved reward learning or punishment learning.

Our detailed analyses of performance help answer an important question - are depressed individuals hyposensitive to reward, hypersensitive to punishment, or both? Hyposensitivity to reward would fit nicely with one of the primary symptoms of depression, anhedonia, which is the inability to experience pleasure from experiences previously enjoyed. Hypersensitivity to punishment could explain the avoidance behaviors also characteristic of depression. Just looking at overall performance on reward and punishment learning, one might be tempted to interpret the larger deficit in

punishment learning as evidence for hypersensitivity to punishment. However, a more detailed look shows convincingly that depressed individuals are less sensitive to positive feedback in these probabilistic reversal learning tasks, and that this is true regardless of whether the task involves learning from rewards or punishments. This shows that a hyposensitivity to reward (including "no punishment" trials in the punishment task) is driving the difference in task outcome, not hypersensitivity to punishment. This information is also important in terms of understanding depression. Depressed individuals may need more help in recognizing and integrating reward and positive information as opposed to decreasing the impact of punishment and negative information.

Why were depressed individuals worse in the punishment task? This could potentially be due to the weak positive feedback signal in the task, which is essentially "no punishment." According to this explanation, depressed individuals are hyposensitive to positive feedback, and perform worse when that positive feedback is the lack of punishment than when that positive feedback is the receipt of a reward.

The computational modeling fits show that depressed individuals were more likely to engage in model-free learning strategies, while controls were more likely to engage in model-based learning strategies. Model-based learning takes into account the structure of the task (specifically, that reward probabilities on the two fractals are anticorrelated). Model-based learning may be associated with more controlled and goal-directed behavior while model-free learning may be associated with more habitual and automatic behavior. Previous studies have shown that model-based learning entails a higher cognitive load, which can be disrupted under the influence of stress. Studies have

found that the stress response attenuates the contribution of model-based but not model-free learning to choice (Otto, Raio, Chiang, Phelps, & Daw, 2013; Otto, Gershman, Markman, & Daw, 2013). Moreover, stress-induced behavioral changes were modulated by individual working memory (WM) capacity, such that low-WM-capacity individuals were more susceptible to detrimental stress effects than high-WM-capacity individuals. An appealing interpretation of our findings, then, is that the psychological stress of depression may interfere with goal-directed or model-based learning, leading depressed individuals to depend on suboptimal model-free learning strategies.

The second difference we observed in our computational model fits was that depressed individuals exhibited a lower learning rate than controls in both the reward and punishment learning tasks. This finding is also supported by the lower percentage of win-stay choices in the depressed group and the linear regression fits. This effect is consistent with the literature suggesting reduced reward responsiveness in depressed individuals. Using probabilistic reinforcement learning tasks, studies have found MDD individuals, compared to controls, show significantly reduced reward responsiveness (Eshel & Roiser, 2010; Pizzagalli et al., 2005; Pizzagalli et al., 2008). In one study, trial-by-trial probability analyses revealed that MDD subjects were impaired at integrating reinforcement history over time and developed a weaker response bias toward the stimulus with a higher reward probability (Pizzagalli et al., 2008).

Finally, although not measured directly in the current study, the current results suggest neurobiological implications. Reinforcement learning has been associated with dopaminergic signals and the prefrontal cortical and striatal targets of those signals.

Studies support attenuated striatal function in depressive pathology across multiple cognitive tasks, from higher-order planning to gambling (Eshel & Roiser, 2010; Price & Drevets, 2009). Interestingly, one study found impaired reward (but not punishment) reversal behavior in depression alongside attenuated ventral striatal response to unexpected reward (Robinson, Cools, Carlisi, Sahakian, & Drevets, 2012). Another study found that reduced ventral striatal responsiveness to unexpected rewards predicted the severity of depression across both unipolar and bipolar depressed groups (Satterthwaite et al., unpublished). Will specific computational deficits in reinforcement learning tasks capture this aspect of reward responsiveness or anhedonia across disorders, and if so, is this linked to common ventral striatal dysfunction? A key priority for future research should be to more closely link these neural and behavioral effects of depression, as well as to explore these effects across a wider range of disorders where blunted reward responsiveness is a key component, including across mood disorders (unipolar and bipolar depression) and psychotic disorders that share the common symptom of anhedonia (Gold, Waltz, Prentice, Morris, & Heerey, 2008; Waltz, Frank, Robinson, & Gold, 2007).

The results need to be interpreted in light of a couple of limitations. Though many patients were referred from depression clinics, we do not have inter-rater reliability for the depression diagnosis. We did not look at treatment and drug effects. Although we did not screen out individuals comorbid with bipolar, substance abuse and/or psychotic symptoms, we did not take other co-morbidity issues into account. Though we matched the groups on IQ, we did not include IQ in the analyses. Working memory, another

potential confound, was also not measured in the present study. There may be other, unmeasured, confounds that differ between the two groups.

In addition, the current research does not address the causal relationship between depression and reward learning. The current study establishes an association, but whether impaired reward learning is a pre-existing risk factor for depression or an effect of depression remains unanswered. Future research could address this question with longitudinal studies or treatment studies. Longitudinal studies would track reward learning performance and onset of depression over a period of time to determine whether the onset of depressive symptoms leads to reward learning impairment or whether impaired reward learning prefaces depressive symptoms. An unselected sample would be necessary to carry out this study. Treatment studies would measure reward learning impairment pre and post treatment of depression. An improvement in reward learning performance for individuals with depressive symptoms in remission would imply depression causes reward learning impairment as opposed to vice versa (Pizzagelli et al., 2013).

GENERAL DISCUSSION

The current research aimed to understand the scope of decision making in psychopathology. Study 1 answered the basic question of whether or not decision-making is impaired in mental illness populations. Two meta-analyses were conducted of studies that used the Iowa Gambling Task (IGT) to assess value-based decision-making in mental illness populations. In the first meta-analysis we compared IGT performance in healthy populations and populations with mental illness. In the second meta-analysis we examined raw IGT performance scores as a function of type of mental illness. The first meta-analysis demonstrated that individuals with mental illness performed significantly worse than healthy control individuals. The second meta-analysis demonstrated no performance differences based on disorder type. These findings suggest that value-based decision-making is a promising target for transdiagnostic analyses of processes that go awry in mental illness but is not sensitive enough to differentiate within disorders.

Study 2 aimed to address two objectives based on the performance of a clinical sample of MDD patients on a number of value-based decision-making tasks. First, we wanted to identify potential dimensions of decision making worth further investigation, and, second, to assess whether decision-making could serve as a potential predictive diagnostic tool. Depressed individuals' decision-making performance was found to be significantly different across a range of decision tasks. Of the decision tasks, punishment learning and a pessimism bias were significant predictors of depression. Decision tasks significantly predict depression but are far outperformed by self-report measures as predictive diagnostic tools. Overall results suggest decision tasks could function as

identifying processes gone awry rather than diagnostic prediction of psychopathology. Thus decision-making may serve as identifying behavioral signatures of psychopathology such as learning and bias in depressed individuals.

Based on the results of study 2 and literature supporting impaired reinforcement learning in clinical depression, study 3 examined the underlying causes of impaired reinforcement-based learning in depressed patients using computational reinforcement learning models. From a performance perspective, the results suggest that depression is characterized by a hyposensitivity to reward and *not* hypersensitivity to punishment. The computational model analyses led to two important findings. First, model free reinforcement learning best accounted for learning in depressed individuals while model-based learning best explained choice behavior of control individuals. Second, depressed individuals had a significantly lower learning rate than controls. These results are promising for the emerging field of computational psychiatry and demonstrate the potential and scope of using decision-making to understand and explain psychopathology from a behavioral perspective.

The above series of studies extends the current state-of-art in a number of ways. Study 1 quantitatively reviewed and demonstrated that decision-making is indeed impaired in mental illness populations. Interestingly enough, no differences were detected within the mental illness populations. This was surprising given the severity and range of population from unipolar depression to psychotic disorders and personality disorders. However, the mental illness group did perform better than organic lesion populations as

expected. Overall from an NIMH process perspective, decision-making may be considered a potential candidate worth further investigation within disorders.

The lack of within mental illness group differences was addressed somewhat in study 2 by investigating a number of value based decision-making tasks within a specific disorder. Our goal was to determine whether decision-making could be treated as one process or whether there were dimensions within the process that would further delineate areas of potential impairment in decision-making for a specific population, in this case clinical depression. We found depressed individuals performed significantly differently across a range of decision-making tasks but certain tasks resulted in more robust differences than others. Reinforcement learning, social decision-making and bias were the strongest contenders. Not surprisingly there is research evidence supporting these findings specifically in depressed individuals.

Investigating the underlying causes of reinforcement learning impairment lead to study 3. Studies have demonstrated that possible reasons for impairment could be cognitive deficits or hyper responsivity to punishment or hypo responsivity to reward. Through computational reinforcement modeling we found model free reinforcement learning explained the depressed group choices while model-based reinforcement learning best explained the control group choices. This suggests that the stress of depression could potentially lead to the inability to use more optimal model-based learning strategies. Running multiple models robustly showed the depressed individuals have a lower learning rate suggesting a hyposensitivity to reward.

These findings have implications for current trends in psychopathology research, which is moving away from a symptom-based approach to defining mental illness and moving towards a more process-based one, as prominently exemplified by the RDoC project. However, RDoC advocates for an even more radical approach to studying decision-making and psychopathology than that used in the current study. Instead of the outcome measure being clinically diagnosed depression, RDoC advocates for abandoning clinical categories. What replaces these categories as outcome measures, whether biological correlates or specific behavioral measures or general measures of daily functioning, remains an open question.

Leykin, Roberts and DeRubeis (2011) found that the failure to use adaptive decision-making strategies spontaneously is an important factor in determining the poor quality of the choices made by depressed individuals, and that prompting the use of such strategies improves decision-making considerably. One thing this result suggests is that some deficits in decision-making in depressed individuals might disappear when depressed individuals are sufficiently motivated or expend sufficient effort. Though lack of motivation would be hard to definitively rule out as an explanation for the current results, real incentives were used in the current study to equalize motivation as much as possible. Perhaps more importantly though, the results of Leykin and colleagues suggest that some decision making deficits in depressed individuals can be remediated, a prospect that should be explored in future research using the current decision making tasks.

Overall the three studies highlighted a number of key points. First decision-making is a process worth using as a tool for investigating mental illness. The feasibility of using decision-making as predictive classification tools, though, seems tentative at best. However, process-based research along with computational modeling could quantitatively explain behavior in a more objective and empirically way than self-reports have so far addressed. Future research investigating brain activation along with behavioral performance would further consolidate findings, as would treatment studies that follow decision-making performance in depressed individuals over the course of treatment. In conclusion decision-making is definitely a process worth investigating in mental illness populations as exemplified within a clinically depressed sample.

TABLES

Table 1

Characteristics of Studies Assessing Decision-making Performance in Clinical Population using the IGT

Study name	Clinical Type	Disorder Type	Diagnosis	*N*	Intelligence Assessment	Intelligence Significant	Substance Abuse Exclusion	TBI Exclusion	Hedge's *g*
Adida et al. 2008	Psych	Mood	BiPolar	90	No	NA	No	Yes	-1.08
Adida et al.2011	Psych	Mood	BiPolar	195	Yes	No	Yes	No	-0.57
Barry & Petry, 2008	Psych	Sub	Multiple	168	Yes	No	No	Yes	-0.49
Bechara et al. 1994	Lesion	Frontal	Frontal	50	No	NA	No	No	-1.50
Bechara et al. 2001	Lesion	Frontal	Frontal	45	Yes	No	Yes	No	-1.05
Boeka & Lokken, 2006	Psych	ED	BN	40	Yes	No	Yes	Yes	-0.92
Bolla et al. 2003	Psych	Sub	Cocaine	26	Yes	No	No	Yes	-0.32
Bolla et al. 2005	Psych	Sub	Marijuana	22	Yes	No	No	Yes	-1.16
Borges et al. 2011	Psych	Anx	OCD	118	Yes	Yes	No	No	-0.15
Brogan et al. 2010	Psych	ED	BN and AN	59	No	NA	No	No	-0.94
Cavedini et al. 2001	Psych	PG	PG	60	Yes	No	No	No	-1.24
Cavedini et al. 2002	Psych	Anx	OCD	68	No	NA	Yes	Yes	-0.95
Cavedini et al. 2004	Psych	ED	AN	141	No	NA	Yes	Yes	-0.94
Cavedini et al. 2010	Psych	Anx	OCD	66	No	NA	Yes	Yes	-1.44
Choi et al. 2011	Psych	Schiz	Schiz	48	Yes	No	Yes	Yes	-0.06
Clark et al. 2001	Psych	MD	BiPolar	45	Yes	Yes	Yes	Yes	-0.79
Clark et al. 2003	Lesion	Frontal	Frontal	62	Yes	No	No	No	-1.09
Da Rocha et al. 2011	Psych	Anx	OCD	214	Yes	No	Yes	No	-0.63
Davis, 2011	Psych	ED	BED	191	No	NA	No	No	-0.24
Dolan et al.2007*	Psych	Sub	Multiple	68	No	NA	No	No	-3.15
Dom, et al. 2007*	Psych	Sub	Alcohol	91	Yes	NR	Yes	Yes	-2.28
Easton et al. 2008	Psych	Sub	Alcohol	25	Yes	Yes	No	No	-1.53
Evans et al. 2005	Psych	Schiz	Schiz	38	Yes	NR	No	No	0.00
Forbush et al. 2008	Psych	PG	PG	59	Yes	Yes	No	No	0.00
Fridberg et al. 2010	Psych	Sub	Marijuana	32	Yes	No	No	Yes	-0.95
Gonzalez-Blanch et al. 2008	Psych	Schiz	Schiz	91	Yes	Yes	Yes	Yes	-0.04

Grant et al. 2000	Psych	Sub	Multiple	54	Yes	Yes	No	Yes	-0.60
Grisham et al. 2007	Psych	Anx	OCD	60	Yes	Yes	Yes	No	-0.15
Guillaume et al. 2010	Psych	ED	BN and AN	170	Yes	Yes	No	No	0.00
Haaland & Landro 2007	Psych	PD	BPD	35	Yes	Yes	No	Yes	-1.49
Hanson et al. 2008	Psych	Sub	Multiple	81	Yes	No	Yes	Yes	-0.54
Jollant et al. 2005	Psych	MD	BiPolar	107	Yes	No	No	Yes	-0.29
Kertzman et al. 2011	Psych	PG	PG	108	No	NA	Yes	No	-0.65
Kjome et al. 2010	Psych	Sub	Cocaine	86	Yes	Yes	No	No	-0.81
Lane et al. 2010.	Psych	Sub	Cocaine	33	No	No	No	No	-0.70
Lawrence et al. 2006	Psych	Anx	OCD	79	Yes	No	Yes	Yes	-0.02
Liao et al. 2009	Psych	ED	BN	77	Yes	No	No	Yes	-0.50
Linnet et al 2011	Psych	PG	PG	30	No	NA	Yes	No	0.00
Linnet et al. 2006	Psych	PG	PG	100	No	NA	No	No	-0.34
Loeber et al. 2009	Psych	Sub	Alcohol	84	Yes	No	No	Yes	-0.02
MacPherson et al. 2009	Lesion	Frontal	Frontal	38	No	NA	No	No	-0.89
Malloy Diniz et al. 2009	Psych	MD	BiPolar	89	Yes	No	No	No	-1.09
Malloy-Diniz et al. 2011	Psych	MD	BiPolar	189	Yes	No	No	No	-0.69
Manes et al. 2002	Lesion	Frontal	Frontal	32	Yes	No	Yes	No	-1.28
Martino et al. 2007	Psych	Schiz	Schiz	36	Yes	No	Yes	Yes	-0.60
Martino et al. 2011	Psych	MD	BiPolar	119	Yes	No	Yes	Yes	-0.04
Maurex et al. 2009	Psych	PD	BPD	78	No	NA	Yes	No	-0.37
Mazas et al.2000	Psych	PD	ASPD	53	Yes	No	No	No	-1.10
Miranda et al. 2009	Psych	Sub	Alcohol	60	Yes	Yes	No	No	-0.72
Must et al. 2006	Psych	MD	MDD	50	No	NA	Yes	No	-1.35
Nakamura et al. 2008	Psych	Schiz	Schiz	49	Yes	Yes	No	No	-0.76
Nielen et al. 2002	Psych	Anx	OCD	53	Yes	No	No	No	0.00
Petry et al. 1998	Psych	Sub	Heroin	93	Yes	No	No	No	-0.38
Pirastu et al. 2006	Psych	Sub	Opiate	69	Yes	Yes	No	Yes	-0.67
Premkumar et al. 2008	Psych	Schiz	Schiz	100	Yes	Yes	Yes	Yes	-0.48
Premkumar et al. 2010	Psych	Schiz	Schiz	45	Yes	NR	Yes	Yes	-0.47
Raffard et al. 2011	Psych	Schiz	Schiz	128	Yes	Yes	No	No	-0.46
Ritter et al. 2004	Psych	Schiz	Schiz	35	Yes	No	No	No	-0.74
Rodríguez-Sánchez et al. 2005	Psych	Schiz	Schiz		Yes	No	Yes	Yes	
Salgado et al. 2009	Psych	Sub	Alcohol	61	Yes	No	No	Yes	-0.94
Sevy et al. 2007	Psych	Schiz	Schiz	47	Yes	Yes	No	Yes	-0.35
Shirayama et al. 2010	Psych	Schiz	Schiz	37	Yes	No	Yes	Yes	-0.43
Shurman et al. 2005	Psych	Schiz	Schiz	49	No	NA	Yes	Yes	-1.54

Starcke et al. 2010	Psych	Anx	OCD	45	Yes	No	Yes	Yes	-1.07
Vadhan et al. 2009	Psych	Sub	Cocaine	46	Yes	Yes	No	No	-1.09
Van Toor et al. 2011	Psych	Sub	Multiple	62	No	NA	No	No	-0.94
Wesley et al. 2011	Psych	Sub	Marijuana	32	Yes	No	No	Yes	-0.28
Woicik et al. 2009	Psych	Sub	Cocaine	90	Yes	No	No	Yes	-0.08
Xi et al. 2011	Lesion	Frontal	Frontal	46	Yes	No	Yes	No	-0.92
Yip et al. 2009	Psych	Schiz	Schiz	63	Yes	Yes	Yes	No	-0.70
Zhang et al. 2011	Psych	Sub	Heroin	39	Yes	No	No	No	-0.64

Note. Anx = Anxiety Disorders, AN = Anorexia Nervosa, BED = Binge Eating Disorder, BN = Bulimia Nervosa, ED = Eating Disorders, Lesion = Frontal Lobe Lesions or Ventro Medial Lesions, TBI = Traumatic Brain Injury, Sub = Substance Abuse and/or Dependence, Mood = Mood , PG = Pathological Gambling , Frontal = Frontal Lobe Lesion, PD = Personality Disorders, OCD = Obsessive Compulsive , BPD = Borderline Personality Disorder, ASPD = Anti Social Personality Disorder, NA = Not Applicable, NR = Not Reported MD= Mood Disorder, NR = Not Reported, Schiz = Schizophrenia, Multiple = Multiple Substance Use, MDD = Major Depressive Disorder, * = study excluded as an outlier.

Table 2

Characteristics of Studies Reporting Raw Mean IGT Performance in Clinical Populations

Study Name	Disorder Type	Diagnosis	*N*	Mean IGT Performance	SE
Adida et al. 2008	Mood	Bipolar	45	-1.50	3.94
Alfonso et al. 2011	Substance	Polysubstance	34	-6.72	2.49
Alvarez-Moya et al. 2011	Gambling	Pathological Gambling	88	-1.10	2.75
Barry & Petry, 2008	Substance	Polysubstance	131	2.30	1.76
Bechara et al., 1994	Lesion	Frontal	6	-25.5	11.54
Bechara et al., 1999	Lesion	Frontal	19	-20.67	6.76
Bechara et al., 2000	Lesion	Frontal	10	-10.60	2.4
Bolla et al. 2005	Substance	Marijuana	11	8.47	4.37
Bolla et al. 2003	Substance	Cocaine	13	6.17	7.13
Borges et al. 2011	Anxiety	OCD	101	-3.71	2.08
Clark et al., 2003	Lesion	Frontal	41	-1.07	3.26
da Rocha et al. 2008	Anxiety	OCD	49	-2.29	1.77
da Rocha et al. 2011	Anxiety	OCD	107	-4.96	1.24
Davis et al., 2011	Eating Disorder	Binge Eating Disorder	85	3.92	2.85
Dolan et al. 2007	Substance	Polysubstance	38	-2.10	1.26
Dom et al. 2007	Substance	Alcohol	38	2.40	0.83
Gonzalez-Blanch et al.	Psychotic	Schizophrenia	70	-1.10	3.12
Grant et al. 2000	Substance	Polysubstance	30	10.20	4.70
Grisham et al. 2007	Anxiety	OCD	30	5.28	1.20
Haaland & Landro 2007	Personality	Borderline Personality	20	-9.85	5.44
Jollant et al. 2005	Mood	Bipolar	25	9.20	5.12
Kjome et al. 2010	Substance	Cocaine	66	0.09	2.77
Linnet et al. 2006	Gambling	Pathological Gambling	61	-0.31	3.13
Loeber et al. 2009	Substance	Alcohol	48	0.90	1.16
Malloy-Diniz et al. 2009	Mood	Bipolar	36	-1.03	4.34
Malloy-Diniz et al. 2011	Mood	Bipolar	95	3.89	2.49
Martino et al. 2007	Psychotic	Schizophrenia	21	0.76	6.12
Maurex et al 2009*	Personality	Borderline Personality	48	18.90	4.03
Mazas et al. 2000	Personality	Anti Social Personality	21	2.95	3.79
McNeely et al. 2008	Mood	Major Depressive	6	-3.10	1.22
Miranda et al. 2009	Substance	Alcohol	39	1.43	3.28
Nakamura et al. 2008	Psychotic	Schizophrenia	24	-3.83	5.54
Pirastu et al. 2006	Substance	Opioid	48	11.30	0.91
Premkumar et al. 2008	Psychotic	Schizophrenia	75	4.45	1.39
Premkumar et al. 2010	Psychotic	Schizophrenia	30	2.80	2.16
Ritter et al. 2004	Psychotic	Schizophrenia	20	-5.20	4.41
Rodriguez-Sanchez et al.	Psychotic	Schizophrenia	80	-1.63	3.09
Salgado et al. 2009	Substance	Alcohol	31	1.03	2.62
Sevy et al. 2007	Psychotic	Schizophrenia	27	-5.00	3.46
Shirayama et al. 2010	Psychotic	Schizophrenia	19	-4.74	3.10
Shurman et al. 2005	Psychotic	Schizophrenia	39	1.90	3.01
Starcke et al. 2010	Anxiety	OCD	23	-1.50	5.62
van Toor et al. 2011	Substance	Polysubstance	31	-3.46	4.73
Wesley et al. 2011	Substance	Marijuana	16	-3.38	2.18
Yip et al. 2009	Psychotic	Schizophrenia	42	5.20	4.17

Note. IGT = Iowa Gambling Task, OCD = Obsessive Compulsive Disorder, SE = Standard Error of Mean IGT Scores, * = study excluded as an outlier.

Table 3
Analyses of Moderation for the Between Group IGT studies

Moderator	*n*	Hedge's *g*	95% CI	*Q* (df)	*p*
Diagnosis	63			4.6 (6)	0.60
Obsessive Compulsive Disorder	8	-0.54**	-0.81 to -0.26		
Eating Disorder	6	-0.53**	-0.84 to -0.21		
Mood Disorder	8	-0.70***	-0.98 to -0.44		
Pathological Gambling Disorder	5	-0.46	-0.82 to 0.10		
Personality Disorders	3	-0.90**	-1.39 to -0.41		
Substance Dependence Disorder	19	-0.63***	-0.82 to -0.44		
Schizophrenia	14	-0.45***	-0.68 to -0.23		
Non-personality vs. Personality	63			1.79 (1)	0.18
Non-personality disorder	60	-0.56***	-0.66 to -0.46		
Personality Disorder	3	-0.90***	-1.38 to -0.42		
Intelligence Assessment	63			8.58(1)	0.003**
No	13	-0.86***	-1.07 to -0.65		
Yes	50	-0.51***	-0.61 to -0.40		
Intelligence Significant	50			2.4(1)	0.35
Yes	18	-0.53***	-0.71 to -0.35		
No	30	-0.52***	-0.66 to -0.39		
Substance Use Exclusion	63			1.08 (1)	0.58
Yes	25	-0.58***	-0.74 to -0.41		
No	38	-0.60***	-0.74 to -0.47		
TBI/Neuropsychological Deficits Exclusion	63			1.06 (1)	0.60
Yes	32	-0.58***	-0.73 to -0.43		
No	31	-0.60***	-0.75 to -0.46		
Administration of IGT	63			1.40(1)	0.50
Computer	51	-0.56***	-0.67 to -0.44		
Hand	12	-0.72***	-1.00 to -0.45		
Clinical Population	69			6.57 (1)	0.01**
Lesion	6	-1.10***	-1.48 to -0.72		
Mental Illness	63	-0.58***	-0.67 to -0.48		

Note. n= number of studies, *p<0.05, **p<0.01, ***p < 0.001

Table 4
Analyses of Moderation for the Mean Performance IGT studies

Moderator	*n*	Effect Size	95% CI	*Q* (df)	*p*
Disorder	40			2.32(6)	0.9
Obsessive Compulsive Disorder	5	-1.35	-0.97 to -0.09		
Eating Disorder	1	3.92	-0.70 to 14.86		
Mood Disorder	5	0.9	-4.25 to 6.04		
Pathological Gambling	2	-0.72	-1.18 to 0.14		
Personality Disorders	2	-2.37	-11.54 to 6.80		
Substance Dependence	14	1.72	-1.2 to 4..64		
Schizophrenia	11	-0.28	-3.8 to 3.24		
Non-personality vs. Personality	40			0.38 (1)	0.54
Non-personality Disorder	38	0.57	-1.19 to 2.32		
Personality Disorder	2	-2.33	-11.34 to 6.67		
Clinical Group	44			23.35 (1)	<0.001***
Lesions	4	-14.12	-19.74 to -8.49		
Mental Illness	40	0.45	-1.35 to 2.26		

Note. n= number of studies, ***$p < 0.001$

Table 5
Demographic Characteristics

	Depressed		Control		Significance
	N	%	N	%	*p* value
Gender					.3
Male	27	57.8	33	51.6	
Female	37	42.2	31	48.4	
Ethnicity					.76
African American	34	53.1	33	51.6	
Caucasian	24	37.5	23	35.9	
Asian	4	6.2	7	10.9	
Other	2	3.1	1	1.6	
Education					.31
No High School Diploma	4	6.3	1	1.6	
High School	26	41.3	23	35.9	
Associate's Degree	10	15.9	12	18.8	
Bachelor's Degree	12	19	16	25	
Master's Degree	11	17.5	9	14.1	
Doctoral Degree	0	0	3	4.7	
On Medication					<.001**
Yes	29	45.3	0	0	
No	33	51.6	63	98.4	
Not Reported	1	1.6	1	1.6	
In Therapy					<.001**
Yes	33	51.6	2	2.31	
No	29	45.3	61	95.3	
Not Reported	1	1.6	1	1.6	
	M	SD	M	SD	*p* value
Age	40.45	13.48	38.53	11.73	.4
WASI	101.32	14.63	103.7	14.1	.35
BDI	30.03	10.46	2.9	4.32	<.001**

Note. ** = $p < .001$

Table 6
Decision Task Performance in Depressed and Control Groups

Decision Task	Measure	Depressed			Control			p value
		M	SD	N	M	SD	N	
Risk Uncertainty								
Risk	Safe Choices (%)	56.69	23.07	63	59.12	22.34	64	.55
Ambiguity	50-50 Choices (%)	59.30	26.14	64	68.06	22.64	64	.05*
Learning Task								
Reward	Rich Choices (%)	59.59	9.84	61	63.21	10.80	63	.05*
Punishment	Rich Choices (%)	41.51	9.93	61	35.44	10.81	63	.001**
Ultimatum Game								
Proposer	Minimum for Self ($)	5.39	0.79	64	5.78	1.27	64	.04*
Responder	Minimum for Self ($)	2.95	1.70	64	3.58	1.55	64	.03*
Negative Bias								
Prediction	Probability in %	54.08	23.60	60	64.03	20.46	62	.01*
Winnings	Amount in $	33.74	27.15	60	31.35	21.78	62	.60
Temporal Tasks								
Delay Discounting	Now Choices (%)	67.16	24.89	64	71.06	23.36	64	.36
Persistence								
	Block A (in secs)	13.77	2.82	64	14.74	2.06	63	.03
	Block B (in secs)	12.83	3.54	63	12.87	3.98	64	.96

Note. * $p < .05$ and ** $p = .001$

Table 7

Factor loadings and communalities based on a principal axis factoring analysis with promax rotation for ten value-based decision-making tasks (N = 116)

	Myopia	Persistence	Uncertainty	Bias	Communality
Punishment: Rich Choice	.71				.55
Reward: Rich Choice	.80				.63
Now Choices	- .36				.20
BlockBmin1sec		.85			.32
BlockAmin1sec		.60			.76
Safe Choices			.48		.21
50-50 Choices			.82		.70
Winning Probability				.70	.48
Propose for Self				.22	.10
Accept for Self				-.21	.08

Note. Factor loadings < .2 are suppressed.

Table 8
Eigenvalues from Parallel Analysis of Decision Making Variables

Factor	Actual Eigenvalues for Current Data	Average Eigenvalues for Random Data
1	1.28	.76
2	1.01	.53
3	.54	.39
4	.23	.28
5	.13	.15
6	-.06	.06
7	-.12	-.03
8	-.16	-.12
9	-.30	-.19
10	-.31	-.26

Note. Factors above dotted line were retained in parallel analysis.

Table 9

Summary of Logistic Regression Analysis for Factor Scores Predicting Depressed and Healthy Individuals

	B	S.E.	Wald	Sig.	Exp (B)	95% C.I. for EXP(B)	
						Lower	Upper
Myopia	-.58	.256	5.063	.024	.562	0.00	6.904E+245
Persistence	.147	.281	.275	.600	1.159	0.00	1.819E+145
Uncertainty	.464	.269	2.980	.084	1.590	0.00	.
Bias	.544	.317	2.944	.086	1.724	0.00	.
Constant	.147	.281	.275	.600	1.159		

Table 10

Factor loadings and communalities based on a principal axis factoring analysis with promax rotation for four self-reports (10 including sub-scales) measuring components of depression (N = 125)

	Negative	Positive	Communalities
CS	.95		.77
BS	.90		.85
BNS	.94		.87
CNS	.94		.82
Snaith-Hamilton	-.64		.66
BIS	.54		.34
Self-Esteem	-.53		.40
Reward Responsiveness BAS		.77	.55
Fun Seeking BAS		.83	.70
Drive BAS		.58	.43

Note. Factor loadings < .4 are suppressed. BNS = Behavioral Non-Social avoidance, CS = Cognitive Social avoidance, BS = Behavioral Social avoidance, CNS = Cognitive Non-Social avoidance, BIS = Behavioral Inhibition Scale, BAS = Behavioral Approach Scale.

Table 11
Eigenvalues from Parallel Analysis of Self-Report Variables

Factor	Actual Eigenvalues for Current Data	Average Eigenvalues for Random Data
1	8.86	.95
2	1.20	.73
3	.56	.60
4	.29	.47
5	.17	.37
6	.14	.28
7	.03	.21
8	.01	.12
9	-.02	.05
10	-.03	-.02

Note. Factors above dotted line were retained in parallel analysis.

Table 12

Summary of Logistic Regression Analysis for Self Report Factor Scores Predicting Depression and Healthy Controls

	B	S.E.	Wald	Sig.	Exp (B)	95% C.I. for EXP(B)	
						Lower	Upper
Negative	-4.23	.86	24.16	.00	.01	.003	.08
Positive	.56	.55	1.03	.31	1.75	.59	5.20
Constant	-1.10	.50	4.71	.03	.34		

Table 13

Summary of Logistic Regression Analysis for Decision Task Variables Predicting Depression and Healthy Controls

	B	S.E.	Wald	df	Sig.	Exp(B)	95% C.I.for EXP (B)	
							Lower	Upper
Safe Choices	.00	.01	.13	1	.72	1.00	.98	1.02
Now Choices	.01	.01	.27	1	.60	1.01	.99	1.03
50-50 Choice	-.01	.01	1.10	1	.30	.99	.97	1.01
Reward: Rich Choice	.01	.03	.31	1	.58	1.01	.97	1.07
Punishment: Rich Choice	-.06	.03	5.66	1	.02*	.94	.90	.99
Minimum Accept	.28	.14	3.73	1	.05*	1.32	1.00	1.74
Minimum Propose	.24	.22	1.12	1	.29	1.27	.82	1.97
Winning Probability	.02	.01	3.15	1	.08^	1.02	1.00	1.04
Block A (min1sec)	.15	.13	1.39	1	.24	1.16	.91	1.50
Block B (min1sec)	-.06	.07	.88	1	.35	.94	.82	1.07
Constant	-3.32	3.27	1.03	1	.31	.04		

Note. * = $p \leq .05$, ^ p = .08

Table 14

Summary of Logistic Regression Analysis for significant Decision Variables Predicting Depressed and Healthy Individuals

	B	S.E.	Wald	df	Sig.	Exp(B)	95% C.I. for	
							Lower	Upper
Punishment	-.062	.020	9.647	1	.002*	.940	.904	.977
MinimumAccept	.312	.137	5.172	1	.023*	1.366	1.044	1.787
WinningProbability	.023	.010	5.625	1	.018*	1.023	1.004	1.043
Constant	.074	1.058	.005	1	.944	1.077		

Note. * = $p < .05$

Table 15

Summary of Logistic Regression Analysis for Self Report Predicting Depression and Healthy Controls

	B	S.E.	Wald	Sig.	Exp (B)
BS Total	-.18	.14	1.78	.18	.83
BNS Total	-.17	.22	.63	.43	.84
CNS Total	.07	.15	.18	.67	1.07
CS Total	-.02	.11	.03	.86	.98
BAS: Drive	.04	.16	.06	.80	1.04
BAS: Fun Seeking	-.03	.28	.01	.92	.97
BAS:Reward	-.12	.24	.24	.62	.88
BIS	-.25	.15	2.84	.09^	.77
Snaith-Hamilton	.13	.07	2.94	.08^	1.13
Self-Esteem	.42	.24	3.02	.08^	1.52
Constant	-6.27	7.93	.63	.43	.002

Note. ^ < .09

Table 16

Summary of Logistic Regression Analysis for Trending Self-Report Variables Predicting Depression and Healthy Controls

	B	S.E.	Wald	df	Sig.	Exp (B)	95% C.I.for EXP(B)	
							Lower	Upper
BIS	-.32	.12	6.78	1	.009*	.72	.57	.923
Snaith Hamilton	.20	.06	12.58	1	.000*	1.22	1.09	1.36
Self-Esteem	.56	.19	8.79	1	.003*	1.76	1.21	2.55
Constant	17.57	5.78	9.22	1	.002	.000		

Note. * = $p < .01$

Table 17

Demographic Characteristics

	Depressed		Control		Significance
	N	%	N	%	*p* value
Gender					0.3
Male	27	57.8	33	51.6	
Female	37	42.2	31	48.4	
Ethnicity					0.76
African American	34	53.1	33	51.6	
Caucasian	24	37.5	23	35.9	
Asian	4	6.2	7	10.9	
Other	2	3.1	1	1.6	
Education					0.31
No High School Diploma	4	6.3	1	1.6	
High School Diploma/Technical	26	41.3	23	35.9	
Associates Degree	10	15.9	12	18.8	
Bachelor's Degree	12	19	16	25	
Master's Degree	11	17.5	9	14.1	
Doctoral Degree	0	0	3	4.7	
On Medication					<.001**
Yes	29	45.3	0	0	
No	33	51.6	63	98.4	
Not Reported	1	1.6	1	1.6	
In Therapy					<.001**
Yes	33	51.6	2	2.31	
No	29	45.3	61	95.3	
Not Reported	1	1.6	1	1.6	
	M	SD	M	SD	*p* value
Age	40.45	13.48	38.53	11.73	0.4
WASI	101.32	14.63	103.7	14.1	0.35
BDI	30.03	10.46	2.9	4.32	<.001

Note. ** = $p < .001$

Table 18
Model free vs. model based RL

		Model Free BIC	Model Based BIC
Rewards			
	Combined	12941.91	**12933.34**
	Controls	6225.36	**6111.45**
	MDD	**6708.57**	6764.83
Punishment			
	Combined	13307.75 13212.10	**13212.10**
	Controls	6343.44	**6197.60**
	MDD	**6924.08**	6935.08

Note. The bold values indicate the best fit statistics

Table 19
Comparison of model fit based on parameters in the RL model

	Model Free BIC	Model Based BIC
Reward Learning		
No difference between MDD and Controls	12941.91	12933.34
Different Stimulus Learning Rates	**12910.06**	**12872.44**
Different Action Learning Rates	12951.01	12942.66
Different Persistence	12948.90	12933.91
Different Bias	12951.22	12942.64
Punishment Learning		
No difference between MDD and Controls	13307.75	13212.10
Different Stimulus Learning Rates	**13261.16**	**13150.41**
Different Action Learning Rates	13308.60	13215.37
Different Persistence	13309.25	13205.42
Different Bias	13315.63	13219.08

Note. The bold values indicate the best fit statistics

FIGURES

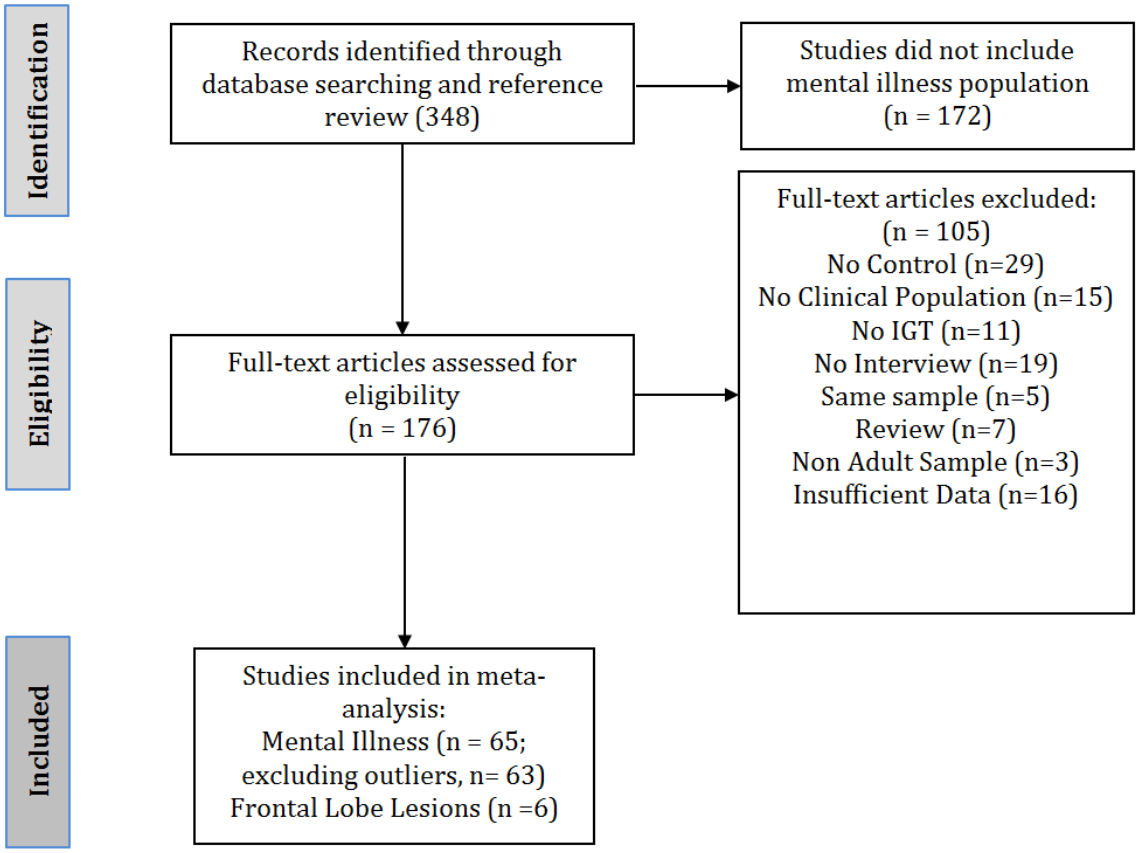

Figure 1. Flow chart illustrating identification of included studies for IGT between group meta-analysis.

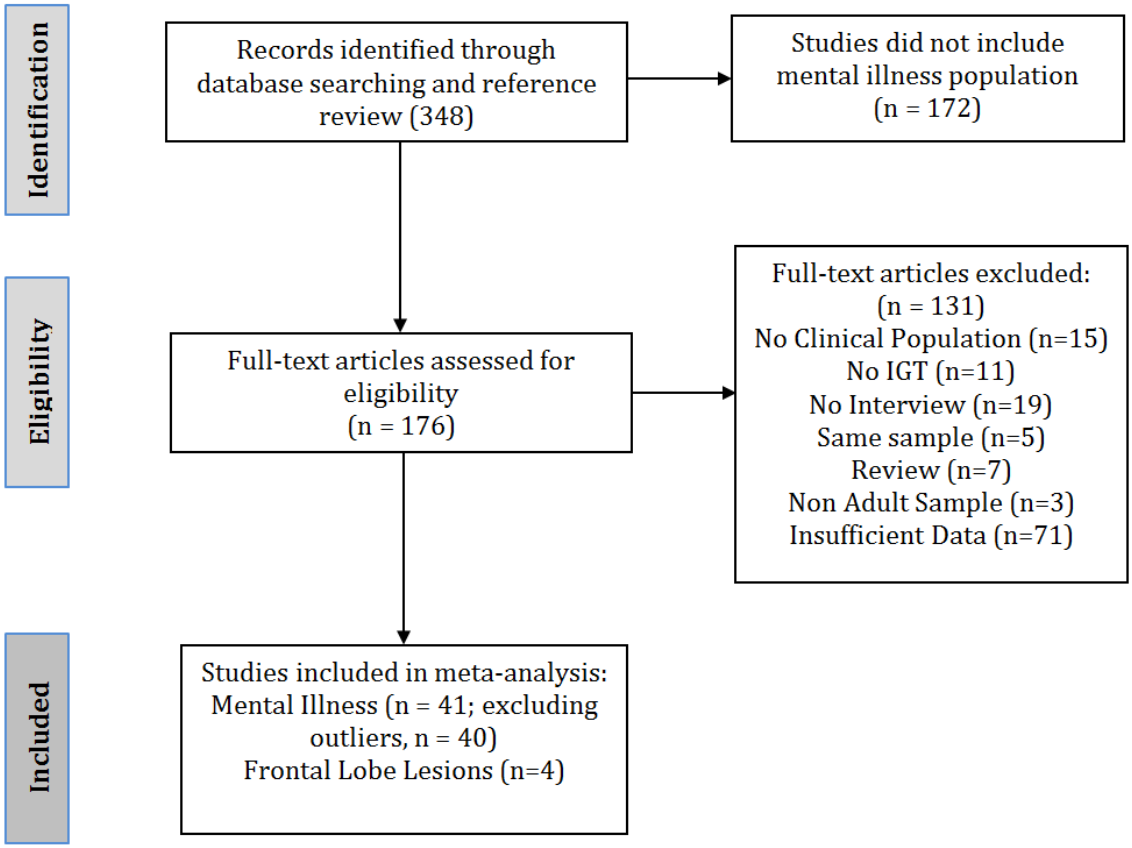

Figure 2. Flow chart illustrating identification of included studies for mean IGT performance meta-analysis.

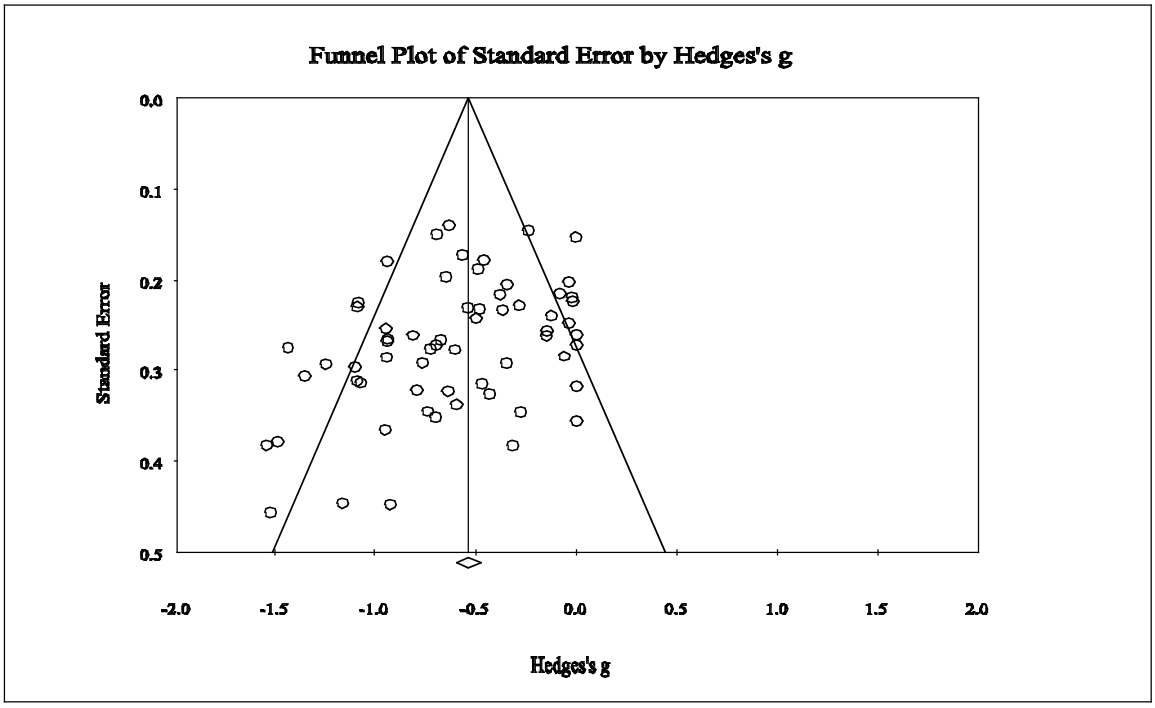

Figure 3. Effect Size Meta-analysis Funnel Plot.

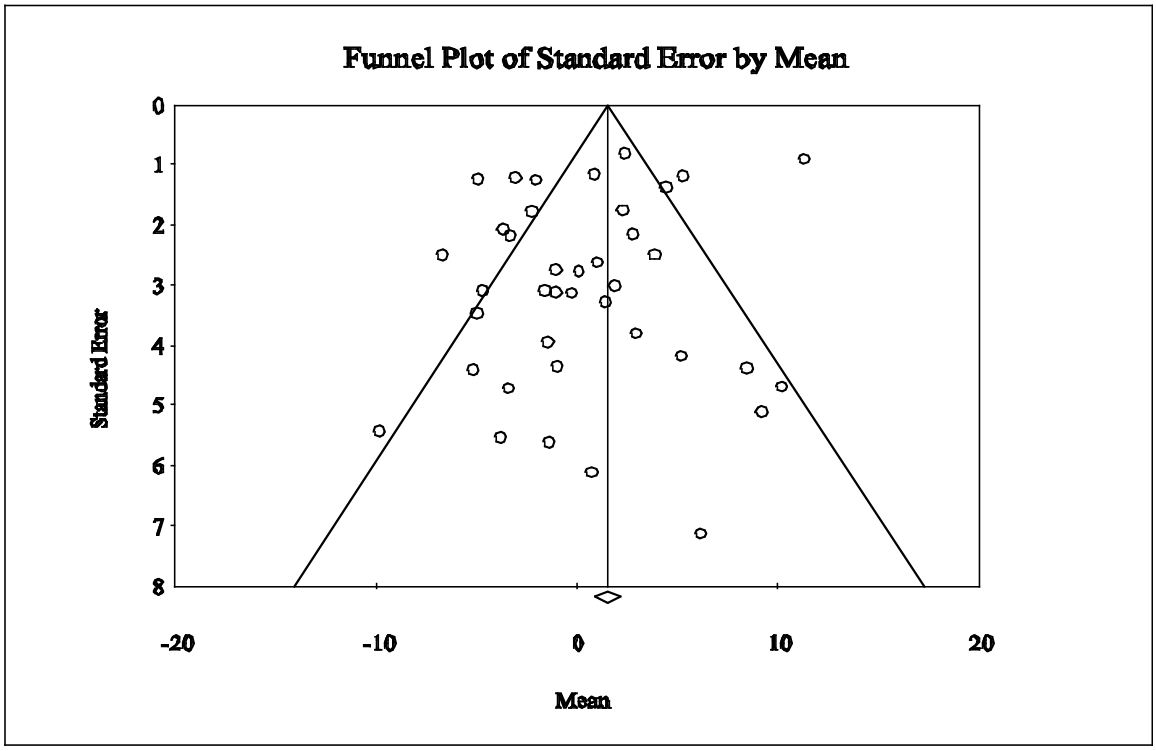

Figure 4. Raw Score Meta-analysis Funnel Plot.

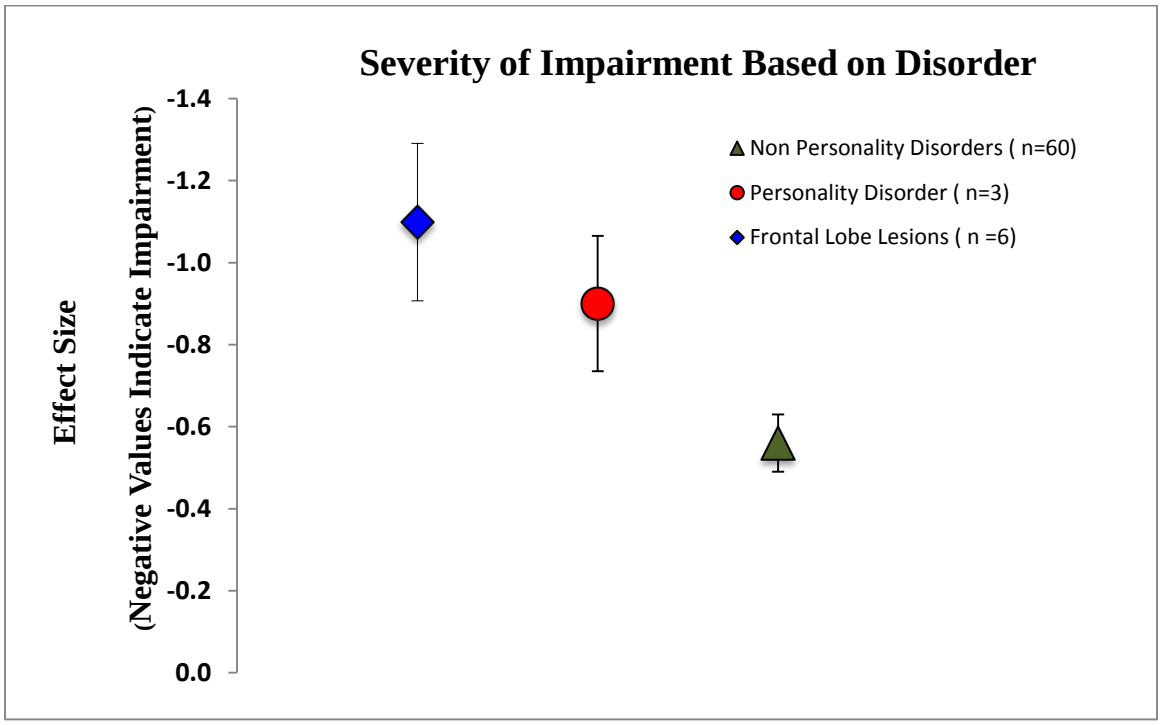

Figure 5. Poor performance on IGT as a function of clinical group, Non Personality Disorders < Personality Disorders < Frontal Lobe Lesions.

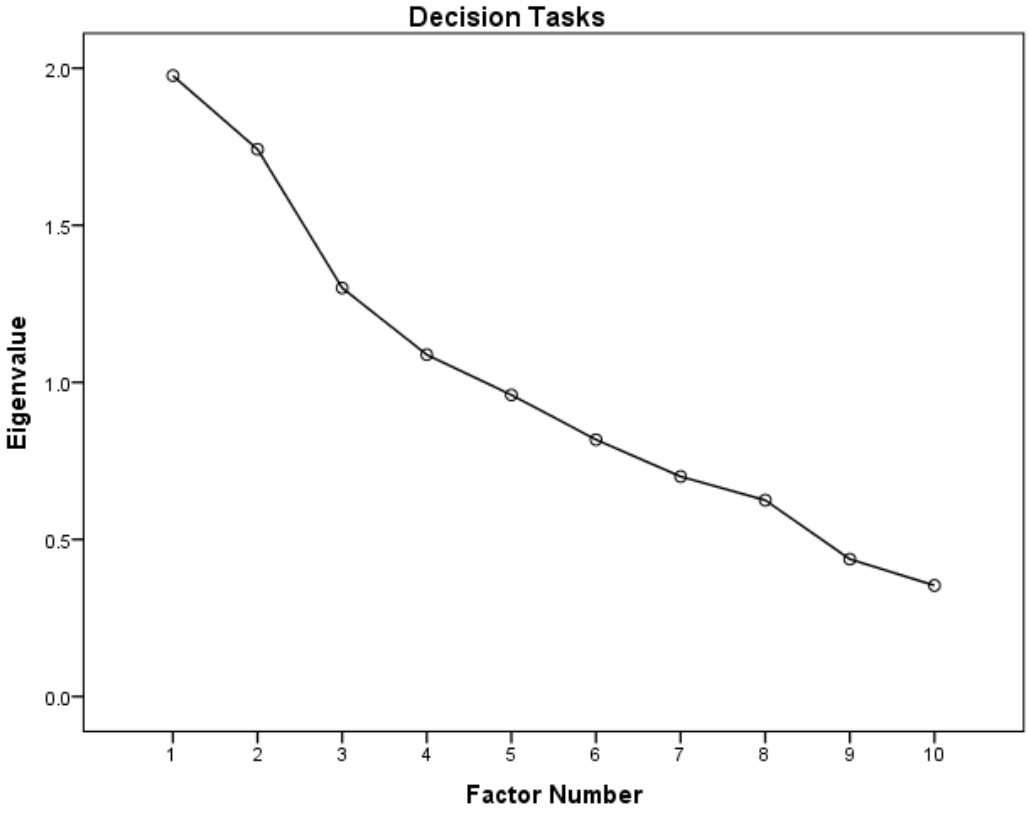

Figure 6. Scree plot for decision task factor analysis indicating a four-factor structure.

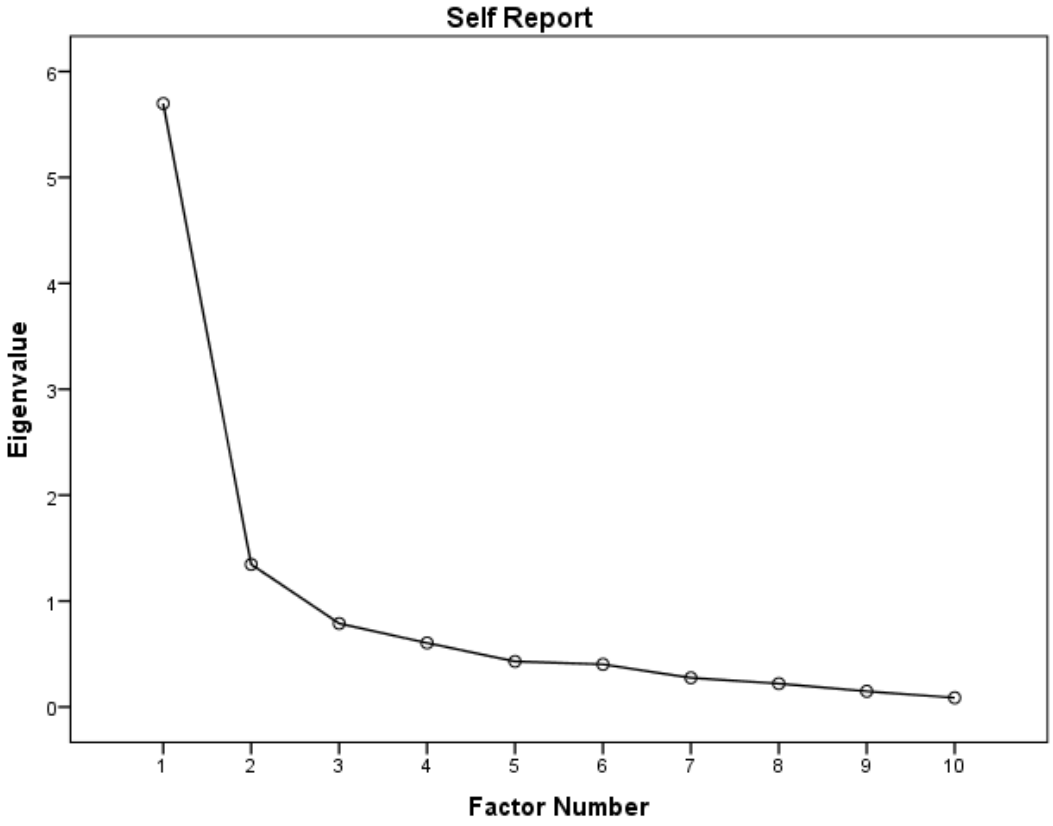

Figure 7. Scree plot for self-report factor analysis indicating a two-factor structure.

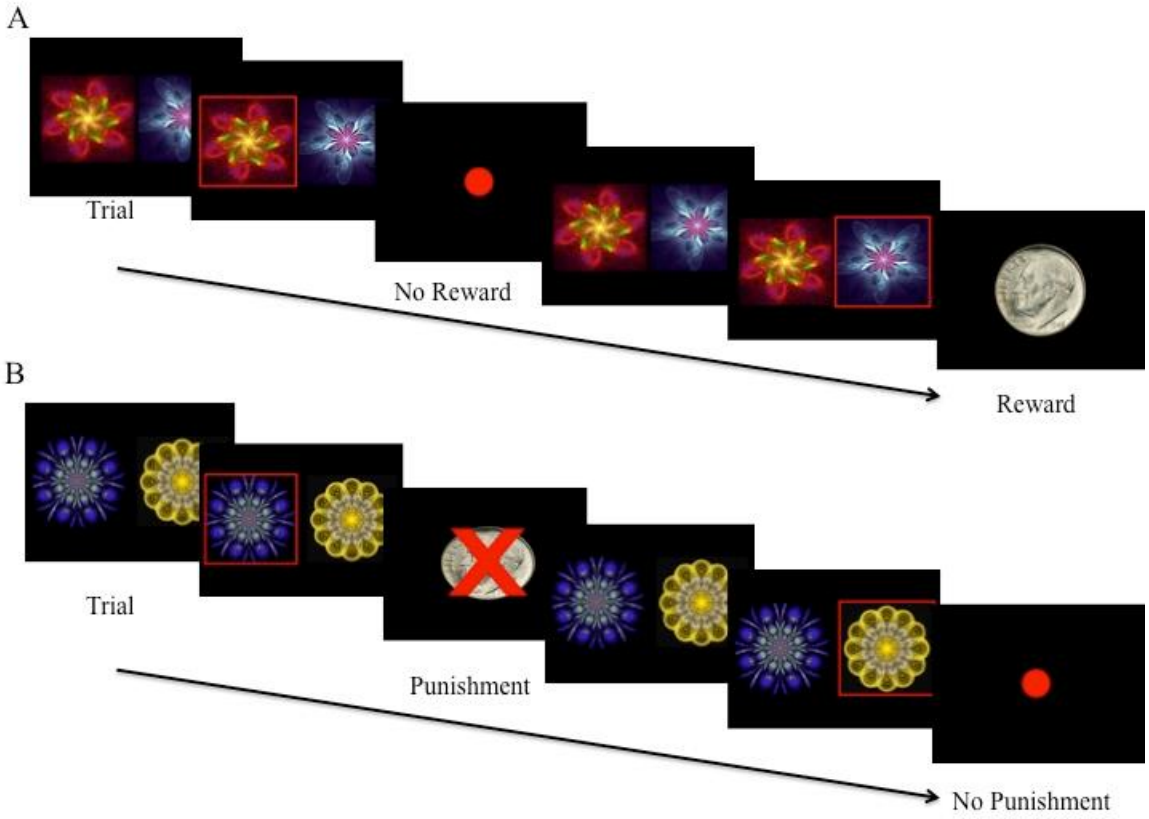

Figure 8. Sequence of events in A. Reward Learning Task and B. Punishment Learning Task.

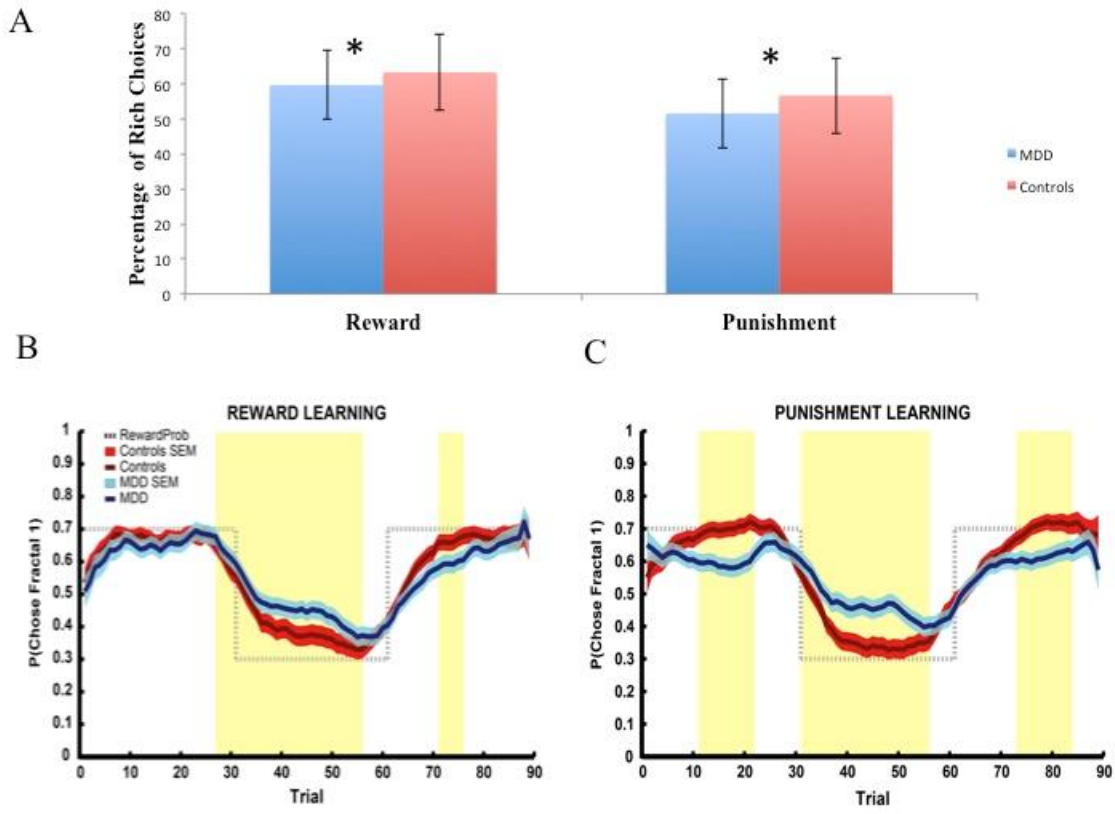

Figure 9. A. Average proportion of rich choices for the depressed and control group in the punishment and reward learning tasks. * denotes $p = <.05$. B. Average proportion of choosing fractal 1 across 90 trials for the depressed and control group in reward learning task. C. Same data as B for the punishment learning task. The shaded areas indicate trials between which depressed group performed significantly worse than control group.

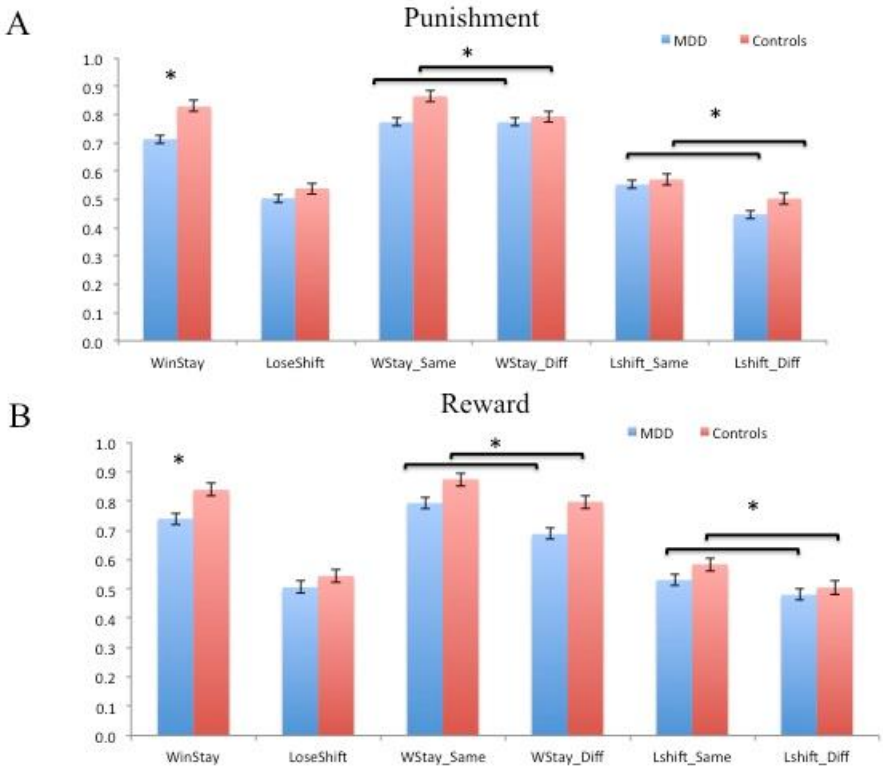

Figure 10. A. Proportion of win-stay, lose-shift, win-stay same side, win-stay different side, lose-shift same side and lose-shift different side choices in punishment learning task, * $p < .05$. B. Proportion of win-stay, lose-shift, win-stay same side, win-stay different side, lose-shift same side and lose-shift different side choices in reward learning task, * $p < .05$.

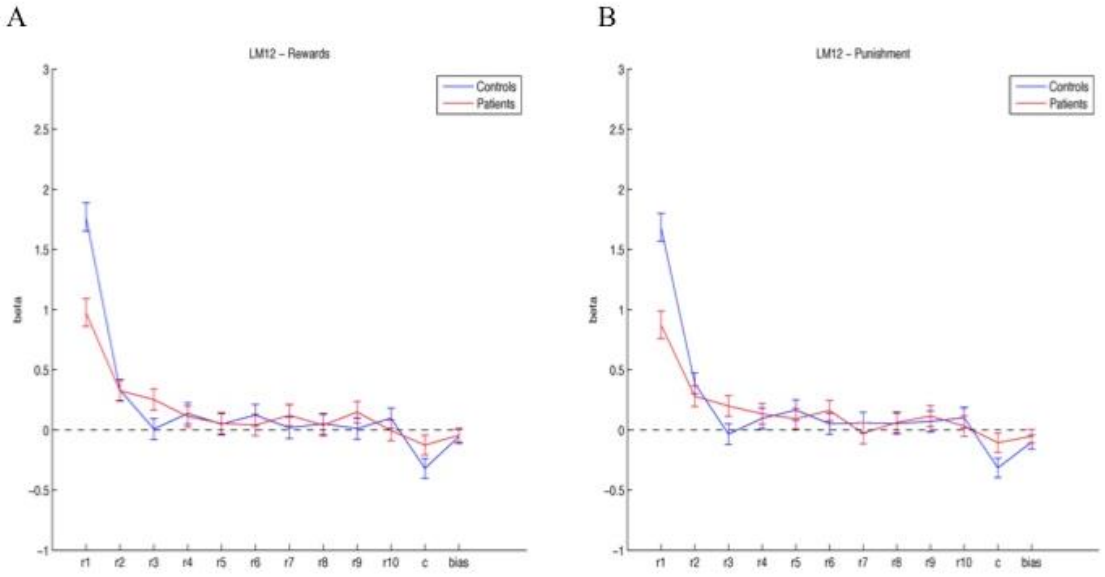

Figure 11. A. Choice behavior as a linear function of reward feedback 10 trials back. B. Choice behavior as a linear function of no punishment feedback 10 trials back.

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